NOT FOR PUBLICATION **FILED UNDER SEAL**

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

AUXILIUM PHARMACEUTICALS, INC. et al., Plaintiffs, v. WATSON LABORATORIES, INC., Defendant.	Civil Action No. 12-3084 (JLL) **OPINION**

LINARES, District Judge**.**

At issue in this case is the validity and enforceability of Plaintiffs' patent for Testim®, a drug commonly prescribed to treat conditions associated with testosterone deficiency in adult males. After careful review and consideration of the evidence presented at a bench trial, the Court finds that Defendant, Watson Laboratories, Inc., has met its burden of proving the invalidity of claim 3 of the '607 patent. Specifically, the Court finds that claim 3 of the '607 patent would have been obvious to a person having ordinary skill in the art at the time the invention was made. The Court also finds that Watson has met its burden of demonstrating that the patent-in-suit is invalid for derivation and/or improper inventorship. Finally, the Court finds that Watson has failed to meet its burden of demonstrating that the '607 patent is unenforceable due to inequitable conduct. This Opinion sets forth the basis for these conclusions.

INTRODUCTION

This is an action for patent infringement arising as a result of Watson's filing of an Abbreviated New Drug Applications ("ANDA") with the U.S. Food and Drug Administration ("FDA") seeking approval to manufacture and sell a generic version of Testim® prior to the expiration of U.S. Patent Nos. 7,608,607 ("the '607 patent"); 7,608,610 ("the '610 patent"); 7,935,690 ("the '690 patent"); and 8,063,029 ("the '029 patent"). Plaintiffs have withdrawn many of their original claims including all asserted claims of the '610, '690 and '029 patents;[1] therefore, the only remaining claim in this litigation is claim 3 of the '607 patent. For the purpose of this litigation, Watson admits that Watson's generic product, if approved, would infringe claim 3 of the '607 patent. Accordingly, the sole issue before the Court is whether Watson has proven that the '607 patent is invalid and/or unenforceable.

This Court has subject matter jurisdiction over this action under 28 U.S.C. §§ 1331 and 1338(a). Venue is proper in this Court under 28 U.S.C. §§ 1391 and 1400(b), and the Court has personal jurisdiction over the parties. On August 14, 2012, the Court entered a "Stipulation and Order Dismissing Defendants Watson Pharmaceuticals and Watson Pharma Without Prejudice." Under the terms of this stipulation, Watson Pharmaceuticals, Inc. and Watson Pharma, Inc. agreed, *inter alia*, to be bound by any stipulation, judgment, order, or decision rendered as to Watson Laboratories, Inc. in the instant matter, including any appeals and any order granting

[1] Pursuant to the parties' October 30, 2014 Stipulation [Docket Entry No. 292], "Plaintiffs have represented that they are no longer asserting infringement of claims 1-2,4, and 9 of the ′607 patent; claims 1-3, 8-12, and 17 of the ′610 patent; claims 1-3 and 7-12 of the ′690 patent; and claims 1, 3-5, and 7-10 of the ′029 patent (collectively, the "Withdrawn Claims") and that the only claim now asserted against Watson in this litigation is claim 3 of the ′607 patent." Thus, the only claim now asserted against Watson in this litigation is claim 3 of the ′607 patent.

preliminary or permanent injunctive relief against Watson Laboratories, Inc., as though Watson Pharmaceuticals, Inc. and Watson Pharma, Inc. were named as defendants in this case.

BACKGROUND[2]

I. The Parties

Plaintiff Auxilium Pharmaceuticals, Inc. ("Auxilium") is a corporation organized and existing under the laws of the State of Delaware, having a place of business at 40 Valley Stream Parkway, Malvern, Pennsylvania 19355. Plaintiff FCB I LLC ("FCB") is a limited liability company organized and existing under the laws of the State of Delaware, having a principal place of business at 1105 North Market Street, Suite 1300, Wilmington, Delaware 19801. Defendant Watson Laboratories, Inc. ("Watson") is a corporation organized and existing under the laws of the State of Nevada, having a place of business at Morris Corporate Center III, 400 Interpace Parkway, Parsippany, New Jersey 07054.

II. The Patent-in-Suit

Plaintiffs Auxilium and FCB filed this action asserting patent infringement against Defendant Watson. FCB is the owner of the '607 patent and Auxilium is the exclusive licensee of the '607 patent. At trial, the patents in dispute were the '607 patent, the '610 patent, the '690 patent, and the '029 patent ("asserted patents"). As previously stated, however, the only remaining claim in this litigation is claim 3 of the '607 patent.

[2] The facts set forth herein are the Court's findings of facts which are based on the Court's observations of the witnesses who testified and a thorough review of all the evidence admitted at trial.

The '607 patent, titled "Pharmaceutical Composition," was duly and legally issued by the United States Patent and Trademark Office ("PTO") on October 27, 2009. Mr. Robert J. Gyurik is listed as the sole inventor of the '607 patent.

The earliest patent application to which the asserted patents claim priority is U.S. Provisional Patent Application No. 60/374,103 ("the '103 provisional application") filed on April 19, 2002.[3]

Mr. Gyurik filed International Patent Application No. PCT/US03/12235 ("PCT '235 application") on April 21, 2003, claiming priority to the '103 provisional application. The PCT '235 application was designated as U.S. Patent Application No. 10/473,724 ("the '724 application") upon filing the United States national stage application with the PTO on October 1, 2003. The PTO issued the '724 application as U.S. Patent No. 7,302,968 ("the '968 patent") on January 22, 2008. Each of the asserted patents claim priority to the '724 application.

Claim 3 of the '607 patent recites:

> 3. A method for maintaining a therapeutically effective concentration of testosterone in the blood serum of a male for treating hypogonadism which comprises transdermally delivering to the male by applying to the skin a composition which is in the form of a topical gel, which has a viscosity of about 500 to about 20,000 cps and a pH of about 3 to about 9, and comprises:
> (A) about 0.1 to about 5 wt. % of testosterone;
> (B) about 0.5 to about 15 wt. % of oxacyclohexadecan-2-one;
> (C) about 0.1 to about 10 wt. % of a thickening agent;
> (D) a mixture of solvents which include:
> (i) about 60 to about 75 wt. % of ethanol or isopropanol; and
> (ii) propylene glycol and glycerin as co-solvents;
> and further comprising polyethylene glycol, wherein the polyethylene glycol ranges from about 0.001 to about 5 wt. %.

(DTX-004).

[3] Thus, pursuant to 35 U.S.C. § 102(b), as discussed below, the critical date for the analysis of prior art to the asserted patents is April 19, 2001.

III. Testim and Testosterone Replacement Therapy

Testosterone is the principal androgen synthesized in the testes. Testosterone is an example of a male steroidal hormone. Testosterone replacement therapy is a form of treatment for hypogonadism. Physicians prescribe testosterone to raise testosterone levels in men who are deficient in it. The most commonly used term for that is hypogonadism. Prior to April 2001, there were several testosterone replacement therapy options available on the market, including: oral products, intramuscular injections, subcutaneousimplants, skin patches, and a transdermal gel. In 2000, the FDA had approved AndroGel® as a topical gel product for the transdermal delivery of testosterone. By April 2001, AndroGel®--which was the only FDA-approved commercially available testosterone gel formulation at that time—had become the most common form of treatment for hypogonadism.

Testim® is a transdermal gel formulation containing 1% testosterone as the active ingredient. Testim® was approved by the FDA by October 31, 2002. Auxilium launched Testim® for commercial sale in the United States on or about February 2003. Testim® is indicated for "testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone." The Testim® formulation is reported in Example 1 of the '607 patent.

A transdermal formulation is generally considered to consist of a drug and a vehicle. A vehicle may contain a penetration enhancer. Penetration enhancers are chemical compounds that are known to sometimes increase permeation of a drug through the skin. The testosterone formulations at issue in this litigation are transdermal gel formulations, which are designed for delivery of testosterone into systemic blood circulation. These transdermal testosterone formulations must achieve adequate delivery of the drug through the skin and into the

bloodstream, so that a sufficient amount of the drug is present in the bloodstream to have a therapeutic effect.

IV. Dr. Dean Hsieh's Work at Conrex

The evidence presented in this case indicates that Conrex Pharmaceutical Corporation ("Conrex") was founded by Dr. Dean Hsieh and his wife, Phyllis Hsieh, in 1985. Ms. Hsieh, who was not a scientist, took over management of Conrex after her husband, Dr. Dean Hsieh, passed away in 1995. Conrex had also employed two Ph.D. level scientists, Dr. Gai and Dr. Casper. Although Conrex collaborated with other companies in connection with its transmembrane research and formulation efforts, none of these collaborations resulted in a commercial product. Dr. Hsieh received two patents, U.S. Patent Nos. 5,023,252 ("the '252 patent") and 5,731,303 ("the '303 patent"), for his permeation enhancement technology. The '252 patent generally claims methods for enhancing drug delivery into and through the skin by applying a composition comprising a particular class of macrocyclic permeation enhancers that includes CPE-215. The '303 patent relates to additional compositions using the same permeation enhancers, including CPE-215. The macrocyclic permeation enhancers described in Dr. Hsieh's patents are referred to as "Hsieh enhancers."

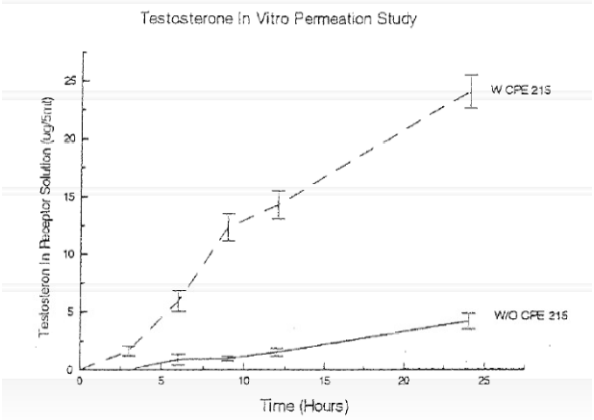
CPE-215 is a trade name for a particular chemical structure that has several chemical names omega-pentadecalactone, cyclopentadecanolide, oxacyclohexadecan-2-one, and Exaltolide. CPE-215 is a macrocyclic enhancer that has a long, flexible ring shaped chemical structure. CPE-215 has long been acknowledged as "Generally Recognized As Safe" or GRAS.

During the course of the trial it was established that, by 1994, Dr. Hsieh had developed several testosterone gels formulations containing CPE-215 as a permeation enhancer, and had tested their *in vitro* permeation using the Franz cell assays. Franz cell tests may test permeation

into and through animal or human skin. Franz cell tests on animal skin (i.e., pigs, hairless rats, or hairless mice) are standard and reliable test, often used "when you want to screen a lot of different formulations." (Trial Tr. 3.110:17-111:1 (Potts)). In an *in vitro* permeation study dated July 20, 1994 ("July 1994 Permeation Study"), Dr. Hsieh tested the permeation of testosterone gels across hairless rat skin. The data from the July 1994 Permeation Study showed that over the course of 24 hours "all three compositions containing the permeation enhancer, the 2, 4, and 8 percent, show substantially greater transport of testosterone through hairless mouse skin, and in particular, the composition containing 8 percent, the TC8, shows the highest transport of all three." (DTX-147 at 6; Trial Tr. 3.136:1-19 (Potts)).

The evidence further set forth that on July 21, 1994, Dr. Hsieh faxed a letter to Dr. Su Il Yum, Senior Director of Product Research, at ALZA Corporation ("ALZA") proposing a joint venture to develop a permeation enhanced testosterone gel. At this time, ALZA "was the premiere company in drug delivery in general and transdermal drug delivery specifically." (Trial Tr. 3.138:11-15, 3.92:19-25 (Potts)). Dr. Hsieh sent ALZA results from Conrex's July 1994 Permeation Study, writing:

> We have been doing work on several hormone replacement products, and thought we'd fax you some recent data on Testosterone showing the effect of our permeation enhancer CPE-215TM (Study Summary attached). We would note that the vehicle in all cases includes 30% Ethanol (w/w), in an aqueous gel also containing Carbomer, Glycerin, Propylene Glycol, Triethanolamine, and Water.



We would be interested in your ideas relating to utilization of our permeation enhanced Testosterone product [in] a fashion of joint development interest to ALZA and to Conrex.

(DTX-211 at 2). In August 1994, Conrex and ALZA executed a Material Evaluation Agreement to test Conrex's CPE-215 (the "Material") with testosterone and estradiol, respectively. Under the terms of the agreement, "ALZA agreed to send its active drugs, estradiol and testosterone (the 'Drugs'), to Conrex," where "Conrex will mix each of the Drugs with [its permeation enhancer] in gel form and ship the resulting gel formulations to ALZA." ALZA would then conduct its own permeation studies and "provide Conrex with a confidential written report summarizing the performance of [its permeation enhancer] in the Studies." (DTX-211 at 21).

On January 25, 1995, about four months later, Dr. Il Yum sent Conrex, as well as "several key individuals at ALZA," the results of its skin flux studies of Conrex's estradiol and testosterone formulations. ALZA had tested the *in vitro* permeation of Dr. Hsieh's testosterone gels across human epidermis skin. The ALZA study showed that the two testosterone gels with CPE-215 (T-2 J2574 and T-4 J2574) exhibited greater flux (rate of speed of drug delivery) across the skin than the gel formulation without CPE-215 (T-0 J2574) at each of the time points measured over the course of 64 hours. Thus, ALZA's study demonstrates that "the gels TC2 and TC4, both of which contain the permeation enhancer, give you a substantially two-fold or greater

increase in the rate of testosterone permeation through human skin from these Conrex gel formulations." (Trial Tr. 3.139:22-3.140:1 (Potts)). No instability was reported in ALZA's results of its permeation studies of Dr. Hsieh's testosterone gels. However, ALZA, a premier transdermal pharmaceutical company, never pursued development of Dr. Hsieh's formulations into commercial products despite the results of its flux studies.

Dr. Hsieh passed away at some point in 1995 from complications of an automobile accident, and his widow, Phyllis Hsieh, subsequently assumed his role as President of Conrex. Dr. Hsieh had not filed for a patent on the testosterone formulations contained in the Permeation Studies prior to his death. At that time, Conrex had only three employees, including Ms. Hsieh.

V. The Conrex Sale to Bentley

At trial, it was established that by the time Ms. Hsieh took over Conrex, the company "focus[ed] on skin care." (Trial Tr. 1.144:11-16 (Hsieh)). Ms. Hsieh had been in discussions with a few companies regarding the sale of certain of its assets, when a consultant representing Bentley Pharmaceutical Corporation ("Bentley") first approached Conrex. Bentley was interested in the pharmaceutical/drug delivery side of Conrex. (Trial Tr. 1.191:6-13, 1.191:14-21, 4.176:17-4.177:2 (Murphy)). In other words, Conrex was interested in the pharmaceutical applications of the CPE-215 technology (e.g., antifungals and hormone replacement therapy). (*Id*. at 4.175:11-177:10). Mr. James Murphy, Bentley's former President and CEO, first met Ms. Hsieh to discuss Conrex's CPE-215 permeation technology in 1995 or 1996. Mr. Murphy and Ms. Hsieh had a second meeting where the discussion "really just focused on the pharmaceutical applications of the [CPE-215] technology." (Trial Tr. 4.176:11-22 (Murphy)).

Mr. Gyurik—who, at that time, was serving as a member of Bentley's Board of Directors—and Mr. Murphy traveled to Philadelphia to visit Conrex's laboratories and offices.

During the one hour meeting in Philadelphia, Mr. Gyurik observed graphical representations of experiments conducted by Conrex, but no documents were provided for his review.

Mr. Murphy and Mr. Gyurik, in turn, prepared an "Executive Summary," dated January 28, 1999, for the Bentley Board of Directors. (DTX-210). The Executive Summary outlined Bentley's objective in obtaining the CPE-215 permeation enhancement technology – "to enhance shareholder value by redirecting the focus of the Company into the Drug Delivery Industry building upon the transdermal and transmucosal technology acquired from Conrex Pharmaceutical Company and to further enhance our standing as one of the top 20 companies in Drug Delivery Systems . . . ." (DTX- 210 at 5). Bentley's mission will be "[t]o generate new, potentially leading, proprietary products that can be licensed out to major pharmaceutical companies who have the ability to commercialize in specific territories . . . ." (*Id.*). To that end, the Executive Summary concluded that that "[t]he proprietary protection of the delivery system will make the new product an attractive asset for commercialization and licensing by providing a less invasive therapy, higher efficacy through elimination of hepatic firstpass metabolism, and improve patient compliance." (*Id.* at 4).

Eventually, the parties entered into an Asset Purchase Agreement. The purchase was structured as a two-part sale with Mr. Yungtai Hsu acting as a middle-man: (i) the Asset Purchase Agreement between Yungtai Hsu and Conrex Pharmaceutical Corporation Dated February 1, 1999, effective as of December 31, 1998; and (ii) the Asset Purchase Agreement between Bentley Pharmaceuticals, Inc. and Yungtai Hsu Dated February 1, 1999, effective as of December 31, 1998 (collectively, the "Asset Purchase Agreement"). "Assets," under the Asset Purchase Agreement, are defined as: (1) Technology; (2) Business Information; (3) Patents; (4) "all Contracts relating to the Patents and Technology that are listed . . . [in] Disclosure

Schedule"; (5) all Licenses; (6) "lists of suppliers and supply agreements, if any"; and (7) "all batch records in existence as of . . . Closing Date." (DTX-45). The Asset Purchase Agreement also contained an assignment of various intellectual property rights, including Conrex's right, title and interest in Patents and Technology. As a result of the purchase, Bentley received two to five boxes from Conrex. Those two to five boxes contained technical information, such as Dr. Hsieh's laboratory notebook, and correspondences with companies, such as ALZA, regarding Dr. Hsieh's CPE-215 permeation technology. Conrex further assigned Bentley the rights to Dr. Hsieh's '252 patent, as well as the rights to his technology, including any and all "information relating to a composition containing a drug and a [Hsieh enhancer]." (DTX-045).

Pursuant to the Asset Purchase Agreement, Bentley agreed to a purchase price of an up-front payment of cash and shares, and "5% of the net profits received by [Bentley] or its successors for fifteen years from the Closing Date from the commercialization of any products developed by [Bentley] or its successors from the Assets." (DTX-045 at 11). This provision of the Asset Purchase Agreement was amended as of December 31, 2007 to provide that Conrex is owed royalties only on any commercial product arising out of a collaboration between Bentley and any of the companies listed on Schedule 2.04(a). (DTX-45 at 159, 46). The December 2007 amendment to the Asset Purchase Agreement also provided that "the parties agree that no royalties are owed to Yungtai Hsu as of the date this Amendment." (DTX-45 at 159).

The skin care side of Conrex continued as a business after the transfer.

On February 26, 1999, less than a month after the close of the Asset Purchase Agreements, Mr. Murphy contacted ALZA seeking to restart the collaborative venture it previously had with Conrex to develop Dr. Hsieh's testosterone gels. Mr. Murphy noted that the

studies conducted by ALZA had indicated "significant activity" in enhancing the delivery of testosterone.

VI. Mr. Gyurik's Development of Testosterone Gel

From 1993 through 1999, Mr. Gyurik worked at MacroChem, during which time he was awarded three U.S. patents related to transdermal formulations resulting from his work and was a co-author of a number of publications, including a chapter on the strategies for transdermal development. After leaving MacroChem, Mr. Gyurik began working at Bentley in March 1999. For more than one year prior to beginning his work with testosterone formulations at Bentley, Mr. Gyurik worked on a number of other projects including antifungal clotrimazole topical delivery formulations, and insulin intranasal delivery formulations.

Once Mr. Gyurik was ready to begin his work on the development of a testosterone gel, he reviewed Dr. Hsieh's lab notebook, containing his Permeation Studies (which, in turn, contained his testosterone permeation data from studies he had conducted on hairless rat skin). Based upon the Permeation Studies, Mr. Gyurik recognized that Dr. Hsieh's goal had been to commercialize a transdermal gel to treat low levels of testosterone in males. Dr. Hsieh's testosterone permeation data provided Mr. Gyurik with some reasonable hope that CPE-215 may function as a permeation enhancer in some formulations, but was not indicative of what would happen in humans with CPE-215 formulations. Further, Mr. Gyurik agreed that ALZA's study of Dr. Hsieh's testosterone gels across human epidermis skin "were also positive, or at least would give somebody hope" that CPE-215 would work with testosterone. (Trial Tr. 3.60:22-61:6, 3.62:25-63:6 (Gyurik)).

Mr. Gyurik started his "first experiment with a testosterone gel at Bentley" by following the directions Dr. Hsieh recorded in his laboratory notebook. In particular, on April 18, 2000—

over 14 months after the Conrex acquisition—Mr. Gyurik made his first attempt to prepare a testosterone gel, labeled TC-4, following the "Conrex procedure" identified in Dr. Hsieh's laboratory notebook "Hormone Penetration." (DTX-146 at 20). Mr. Gyurik replaced 5% testosterone concentration, used in the Permeation Studies, with 1% of testosterone because AndroGel® was a 1% testosterone gel and further changed the type of Carbopol thickening agent and pH-adjusting agent. Mr. Gyurik observed that his experiment formed an "immediate gel." (DTX-146 at 20). Six days later, Mr. Gyurik observed that a "big glob"—having a dry weight of either 2.5 or 25 grams—had formed in the gel he had prepared on April 18, 2000. As a result of the "big glob," Mr. Gyurik concluded that his reproduction of TC-4 was unstable, although he did not indicate as such in his lab notebook. (DTX-146 at 20). Unstable gels are not useable as a pharmaceutical composition. (Trial Tr. 1.134:21-1.135:4 (Lane); Trial Tr. 3.215:18-3.217:23 (Potts)).

After Mr. Gyurik's initial attempt to reproduce Conrex's TC-4 formulation contained within the Permeation Studies resulted in what he described at trial as an unstable formulation, Mr. Gyurik engaged in four more attempts to create a testosterone gel. In his fifth and final iteration, on May 5, 2000, Mr. Gyurik reduced the amount of glycerin, substituted Carbopol 980 NF for 940, and added 0.5% PEG-1000 to reduce tackiness. (DTX-148 at 4, Trial Tr. 2.174:9-14 (Gyurik)). Mr. Gyurik's last iteration "is essentially identical with the Testim® formulation." (Trial Tr. 2.72:12-2.73:2 (Gyurik)). In total, it took Mr. Gyurik "seventeen calendar days" and five iterations from his "first experiment with a testosterone gel at Bentley" to reach the formulation that "is essentially identical with the Testim® formulation." (Trial Tr. 2.40:7-15, 2.72:12-2.73:6 (Gyurik)). Trial testimony established that seventeen (17) days is "an

exceptionally short period of time" for the development of a formulation. (Trial Tr. 3.182:11-16 (Potts); 6.156:25-6:157:4 (Lane)).

VII. Mr. Gyurik's Correspondence Concerning Question Posed by MCA

Dr. Hsieh's permeation studies were the only *in vitro* transdermal data that Mr. Gyurik had to show that Testim® worked before it entered human clinical trials. (Trial Tr. 2.77:20-2.78:8 (Gyurik)). As such, on November 26, 2002, Mr. Gyurik wrote a letter to Ms. Terri Sebree, an executive at Auxilium responsible for regulatory and clinical affairs, responding to a question posed by the MCA (UK Health authorities). By way of background, Ms. Sebree wrote that the MCA had asked "for justification of the Testim formulation and how we developed the formulation." (DTX-153 at 2). Mr. Gyurik responded:

> Following is a response to your question: "*The MCA (UK Health authorities) have asked us for justification of the Testim formulation and how we developed the formulation*"
> **In Vitro Testing**
> Early in the testosterone topical delivery program, various formulations differing in concentrations of both the *key excipient, CPE-215*, and testosterone, the active pharmaceutical ingredient (API) were prepared and tested *in vitro* in Franz diffusion cells. *This was to get an idea of which formulation may work best in an in vivo situation*. Many experiments were conducted with different compositions thus explored; a typical result is shown in the figure below:
> As can be seen, the composition containing 8% CPE-215 (w/w) was numerically better than the other compositions, *so this level of the key excipient was chosen*.

(DTX-153 at 2). The above letter by Mr. Gyurik contained a graph; he did not, however, conduct the testing that provided the results laid out in said graph. (Trial Tr. 2.77:5-7 (Gyurik)). The testing had been done by Conrex. (Trial Tr. 2.76:21-2.77:4 (Gyurik)). Mr. Gyurik understood that the information he provided would be presented to the U.K. health authorities to consider approval for Testim®. (Trial Tr. 2.197:18-198:13 (Gyurik)).

VIII. Patent Prosecution

At Bentley, Mr. Gyurik was a Chair of several committees, including Bentley's Patent Committee. As Chair of the Patent Committee, Mr. Gyurik was responsible for understanding what patents Bentley had, what was transpiring with Bentley's patent applications, and for informing other employees at Bentley about the status of those patent applications.

In this capacity, Mr. Gyurik was involved in the prosecution of the '968 patent, a parent of the application that issued as the '607 patent. (Trial Tr. 3.20:25-3.21:5 (Gyurik)). During the prosecution of the '968 patent, the examiner considered and reviewed, *inter alia*, U.S. Patent No. 6,503,894 ("the '894 Dudley patent"), U.S. Patent Nos. 5,023,252 and 5,731,303 ("the Hsieh '252 patent and '303 patent"), and U.S. Patent No. 5,968,919 ("the '919 Samour patent"), as well as four out of five of the so-called "Bentley Disclosures." (DTX-011 at 373, 765–767; Trial Tr. 4.189:4-20, 4.190:13-22 (Barron); Trial Tr. 4.15:3-22 (Potts)).

As part of the '724 application, Mr. Gyurik submitted a Declaration and Power of Attorney for Patent Application signed on September 9, 2003. In his inventorship declaration, Mr. Gyurik declared:

> As a below named inventor, I hereby declare that . . . I believe I am the original, first and sole inventor . . . of the subject matter which is claimed and for which a patent is sought on the invention entitled PHARMACEUTICAL COMPOSITION the specification of which . . . was filed on April 21, 2003 as . . . PCT International Application Number PCT/US03/12235.

(DTX-011 at 157). In other words, Mr. Gyurik signed and submitted a declaration attesting that he believed he was the "original, first, and sole inventor" of the claimed subject matter for which he was seeking to obtain a patent. (DTX-011 at 157). In particular, claim 1 of the '724 application recited a "pharmaceutical composition comprising: (A) an androgen; (B) a Hsieh

enhancer; and (C) a thickening agent." When Mr. Gyurik signed his inventorship declaration, his patent attorneys, Mr. Alexis Barron and Mr. Gene Yao, specifically brought the declaration to his attention and advised him of his duty of candor and duty to disclose material information to the PTO. In his declaration, Mr. Gyurik declared that he understood his duty to be truthful with the PTO and declared that "that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true." (DTX-011 at 158). Mr. Gyurik also declared that he understood his "duty to disclose to the United States Patent and Trademark Office all information known to me to be material to patentability." (DTX-011 at 158; Trial Tr. 3.13:17-14:20 (Gyurik)).

The "Abstract" of the original patent specification in the '724 application states: "A pharmaceutical composition comprising: (A) an androgen, (B) a cyclic enhancer of the type used in the compositions and methods claimed by U.S. Patent No. 5,023,252 to Hsieh; and (C) a thickening agent; including, for example, a composition in which the cyclic enhancer is a macrocyclic ester or a macrocyclic ketone; the use of the composition to treat a condition, for example, male hypogonadism, in a patient by applying the composition to the membrane of the patient; and a method for making the composition." (DTX-011 at 153). Having received and reviewed Dr. Hsieh's lab notebook and Permeation Studies in or about April 2000, Mr. Gyurik knew—before he submitted the '724 patent application, in September 2003—that Dr. Hsieh had prepared a transdermal gel formulation comprising (a) an androgen; (b) a Hsieh enhancer; and (c) a thickening agent. However, having detected physical instability in his reproduction of Dr. Hsieh's TC-4 formulation, Mr. Gyurik believed that said formulation, contained in the Permeation Studies, was a failure and thus would not be suitable for use in humans as pharmaceutical composition.

During prosecution of the '968 patent, a parent of the application that issued as the '607 patent, the examiner considered and reviewed, *inter alia*, U.S. Patent No. 6,503,894 ("the '894 Dudley patent"), U.S. Patent Nos. 5,023,252 and 5,731,303 ("the Hsieh '252 patent and '303 patent"), and U.S. Patent No. 5,968,919 ("the '919 Samour patent") as well as four out of five of the so-called "Bentley Disclosures."

On February 15, 2007, the PTO issued its first rejection of Mr. Gyurik's original patent application. The PTO found that it would have been obvious to modify a permeation-enhanced testosterone gel formulation as taught by the Dudley patent (the '894 patent) to include a Hsieh enhancer as taught by the Hsieh patent (the '252 patent):

> Dudley et al. teaches a transdermal unit dose androgenic gel and a method for treating hypogonadism by placing the composition on the shoulder or upper arm where it dries . . . . The gel comprises an androgen, an alcohol (e.g. ethanol), a penetration enhancer, a thickener, water, and optionally include salts, emollients, stabilizers (embracing crystallization inhibitors and neutralizing agents – see dictionary definition in References), antimicrobials, fragrances, and propellants (Col. 12, lines 17-22).
> . . . .
> Dudley does not teach the use of an Hsieh enhancer, such as oxycyclohexadecan-2-one [sic]. Hsieh (U.S. Patent No. 5,023,252) teaches a new class of enhancers, primarily macrocyclic enhancers. Thus, it would be obvious to one of ordinary skill in the art at the time the invention was made, to modify the composition taught by Dudley to include the enhancer taught by Hsieh.

(DTX 11 at 777-780).

On April 30, 2007, Mr. Gyurik's patent counsel filed a response to the PTO's February 17, 2007 rejection. In the "Summary of the Invention" section, the response stated: "The present invention relates to pharmaceutical compositions useful for the delivery of androgen to a subject. The compositions comprise: (A) an androgen; (B) a cyclic enhancer of the type disclosed by U.S. Patent No. 5,023,252 to Hsieh; and (C) a thickening agent." (DTX at 812). The April 2007

response argued that the pending claims were not obvious over the combination of the Dudley and Dr. Hsieh's '252 patent because there was no motivation to include a Hsieh enhancer in the permeation-enhanced testosterone gel disclosed in the Dudley patent. In particular, Bentley's patent counsel explained that there was "no evidence in [the Dudley] patent that [the Dudley inventors] considered the disclosure of the Hsieh patent as being relevant to their work," Hsieh does not teach "the use of the enhancer described therein with an androgen [e.g., a male hormone]" and thus, there was no motivation in Hsieh's '252 patent to use an androgen (testosterone), and "[g]iven the state of the art respecting the difficulty of combining an androgen with any given enhancer, it is manifest that the present record contains no such showing to provide the [POSA] with a reasonable expectation of success." (DTX-011 at 821-824). The '968 patent issued on January 22, 2008. (DTX-001).

During the prosecution of the '607 patent, on April 27, 2009, the PTO rejected all pending claims as obvious over the Dudley patent in view of the Hsieh patent. (DTX-014 at 191-93). The PTO found that "[g]iven the improved enhancing properties of the Hsieh transdermal delivery enhancers over the enhancers of Dudley et al., it would be obvious to substitute the improved enhancer as a means of improving delivery where the testing disclosed in Hsieh provides a reasonable expectation of success." (*Id*. at 192-193). In response to the April 2009 rejection, Mr. Gyurik's patent counsel argued that the pending claims should be allowed because the patentee successfully overcame "a similar obviousness rejection [over the Dudley and Hsieh patents that] was made in the parent application that issued as U.S. Patent No. 7,320,968." (Id. at 270). The PTO issued the '607 patent to Mr. Gyurik on October 27, 2009.

The PTO issued a similar rejection and Mr. Gyurik's attorneys filed a similar response during the prosecution of the '610 patent, the '690 patent, and the '029 patent. The PTO issued

the ’610 patent on October 27, 2009, the ’690 patent on May 3, 2011, and the ’029 patent on November 22, 2011.

Mr. Gyurik understood that he owed a duty of candor and a duty to disclose material information to the PTO. He had a familiarity with the basic patent criteria of utility, novelty, and non-obviousness at the time.

In an un-dated memo, entitled “Testim patent expansion issues,” Mr. Gyurik’s “points” emphasize the need “to distinguish [our patent claim] from the original Hsieh patent” for patentability:

> Our patent claim we need three things (testosterone, CPE-215 and PEG) all together to make the formulation work. (Why? First, because we have to distinguish it from the original Hsieh patent; second, we do need crystallization inhibitor to have near zero order release profile.) Any more work we do will undermine our patent position.

(DTX-166; Trial Tr. 3.31:23-3.32:5, 3.33:1-8 (Gyurik)).

The PTO reviewed the asserted patents and their related applications over the course of a decade. In that time, Mr. Gyurik did not disclose to the PTO Dr. Hsieh’s Permeation Studies because, as previously stated, having detected physical instability in his reproduction of Dr. Hsieh’s TC-4 formulation, Mr. Gyurik believed that said formulation, contained in the Permeation Studies, was a failure and thus would not be suitable for use in humans as pharmaceutical composition.

IX. Mr. Gyurik’s Retirement

Mr. Gyurik retired from Bentley in 2008, which was before the prosecution and issuance of any of the asserted patents, except for the ’968 patent—which issued on January 22, 2008. (Trial Tr. 3.189:19-21 (Gyurik)). Although Mr. Gyurik did not receive any financial compensation for being named the sole inventor of any the patents, nor was he receiving any

royalties or compensation for the continued validity of the patents, at around the same time of his retirement and the issuance of the first Testim® patent, Mr. Gyurik received "between one and three million" dollars from the sale of Bentley Spain to Teva. The Testin® assets were excluded from the Bentley Spain/Teva transaction and were, instead, spun out into a separate entity called CPEX. After Mr. Gyurik retired from Bentley, CPEX retained Mr. Gyurik as a consultant.

X. Obviousness

A. The Experts

Watson's expert, Dr. Russell Owen Potts, is an expert in the field of research and development for the delivery of active pharmaceutical ingredients into and through the skin. He has over thirty years of experience in this field. He has led teams at various drug companies, including Pfizer and Cygnus, in drug development. He has also contributed to the research and development of several FDA approved transdermal products, including steroidal hormones. He has vast experience in formulating gel products that are topically applied to the skin for delivery of drugs into and through the skin. Dr. Potts has been awarded 35 patents and is recognized as a leader in the field, most notably to serve as the Chairman of the Gordon Conference on topical and transdermal drug delivery.

Plaintiffs have retained the following experts: (1) Dr. Lane, (2) Dr. Morgentaler, and (3) Dr. Levin. Dr. Majella Lane is an expert in transdermal drug formulation and delivery. Dr. Lane's research predominantly focuses on the area of transdermal delivery of pharmaceutical products. She has been working in the general field of membrane permeation for the past 22 years during which time she has been intimately involved with industrial research in the area and has been a consultant to numerous multinational companies. Dr. Lane was the Director of the Masters of Science Program in Pharmaceutical Technology at Trinity College, Dublin, from

1997 to 2005, where she supervised over 30 postgraduate students who were funded by a variety of sources, including research councils, governments, and industry. The program was organized in collaboration with Elan Pharmaceuticals to specifically develop the skill set of the employees of Elan in the area of formulation technologies for different routes of drug delivery, including the transdermal route of delivery. Since 2005, Dr. Lane has held the titles of Senior Lecturer in Pharmaceutics and Director of the Skin Research Group at the School of Pharmacy, University College London. She is also a Visiting Scientist in the Department of Pharmaceutical Sciences, College of Pharmacy, University of Michigan.

Dr. Morgentaler is an expert in the field of clinical research and treatment of testosterone deficiency. He is the Director of Men's Health Boston, one of the first health centers in the United States dedicated to treating the special medical needs of men, specifically hypogonadism, infertility, vasectomy and vasectomy reversal, prostate conditions, and sexual dysfunction. Dr. Morgentaler received his A.B., magna cum laude, from Harvard College in 1978, and earned his M.D. in 1982 from Harvard Medical School. He completed internships and residencies in surgery in the Harvard Surgical Service, New England Deaconess Hospital from 1982 to 1984, and urology, in the Harvard Program in Urology from 1984 to 1988. Dr. Morgentaler is licensed and board-certified urologist specializing in men's health issues, such as testosterone deficiency, sexual dysfunction, and infertility. Between 1987 and 1988, Dr. Morgentaler held the position of Chief Resident of the urology program. He became an Instructor in Surgery (Urology) at Harvard Medical School from 1988 until 1993, when he then rose to the position of Assistant Professor, which he held until 1998, at which time he was promoted to Associate Professor. Subsequently, in 1999, he became Associate Clinical Professor of Urology, a position he currently holds today. He also teaches a course on testosterone therapy and male reproduction in

the Health Sciences and Technology program, a collaboration between Harvard Medical School and the Massachusetts Institute of Technology. Dr. Morgentaler has published extensively on hypogonadism based on his research and clinical experience, including authoring or co-authoring over 125 journal articles, 10 book chapters, four books, and other materials in the field of urology relating to men's health. Dr. Morgentaler was the only clinician to testify at trial

Finally, Dr. Levin is an expert in biostatistics, statistical methods in epidemiology, the analysis of categorical data, and the design of clinical trials. He has held the rank of Full Professor with tenure since 1994 in the Department of Biostatistics at the Mailman School of Public Health of Columbia University and served as the Chair of the Department for over eleven years. In addition to his work at Columbia University, Dr. Levin has consulted with the United States Food and Drug Administration, the National Institute of Health, and with pharmaceutical companies such as Johnson & Johnson, Eisai, Pfizer, SmithKline Beecham, and Sanofi-Aventis concerning the design and analysis of clinical trials. Dr. Levin received his B.A. in Mathematics from Columbia College in 1968, his M.A. in Mathematics from Harvard University in 1972, and his Ph.D. in Applied Mathematics/Statistics also from Harvard University in 1974. His academic work entails teaching biostatistics to medical and public health students, consulting with biomedical researchers at the Columbia University Medical Center, and publishing research papers of his own in mathematical statistics. Dr. Levin has published over 170 articles, reviews, chapters, columns, technical reports, and other materials in prestigious journals such as the New England Journal of Medicine. He is also a co-author of three books on statistics.

LEGAL ANALYSIS

Watson argues that claim 3 of the ′607 patent is: (1) invalid for obviousness; (2) invalid for improper inventorship and derivation; and (3) unenforceable due to inequitable conduct. Because all patents "shall be presumed valid," 35 U.S.C. § 282, the "burden is on the party asserting invalidity [here, Watson,] to prove it with facts supported by clear and convincing evidence." *Linear Tech Corp. v. Int'l Trade Comm'n*, 566 F.3d 1049, 1066 (Fed. Cir. 2009) (internal citations omitted).

I. Patent Invalidity

A. Obviousness

"An obviousness analysis measures the difference between the claimed invention and the prior art to determine whether 'the subject matter as a whole would have been obvious at the time the invention was made' to a person having ordinary skill in the art." *Unigene Labs., Inc. v. Apotex, Inc.*, 655 F.3d 1352, 1360 (Fed. Cir. 2011). Obviousness is a question of law based on underlying factual findings. *Honeywell Int'l, Inc. v. United States,* 609 F.3d 1292, 1297 (Fed. Cir. 2010). "The factual underpinnings, often referred to as the *Graham* factors, include 1) the scope and content of the prior art; 2) the level of ordinary skill in the art; 3) the differences between the claimed invention and the prior art; and 4) evidence of secondary factors, also known as objective indicia of nonobviousness." *Id.* at 1360.

"Obviousness requires more than a mere showing that the prior art includes separate references covering each separate limitation in a claim under examination. Rather, obviousness requires the additional showing that a person of ordinary skill at the time of the invention would have selected and combined those prior art elements in the normal course of research and development to yield the claimed invention." *Unigene*, 655 F.3d at 1360. Moreover, the party

challenging validity must show that a person of ordinary skill in the art "would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and . . . would have had a reasonable expectation of success in doing so." *Procter & Gamble v. Teva Pharm.*, 566 F.3d 989, 994 (Fed. Cir. 2009) (quotation omitted). A claimed invention may, however, be obvious even when the prior art does not teach each claim limitation, so long as the record contains some reason that would cause one of skill in the art to modify the prior art to obtain the claimed invention. *Beckson Marine, Inc. v. NFM, Inc.*, 292 F.3d 718, 728 (Fed. Cir. 2002). A finding of obviousness cannot, however, be based on "the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention." *Crown Operations Int'l, Ltd. v. Solutia, Inc*., 289 F.3d 1367, 1376 (Fed. Cir. 2002) (quoting *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534, 546 (Fed. Cir. 1998)).

"A person of ordinary skill at the time of the invention interprets the prior art using common sense and appropriate perspective." *Unigene*, 655 F.3d at 1361; *see generally KSR Int'l Co. v. Teleflex Inc*., 550 U.S. 398, 420-421 (2007) ("A person of ordinary skill is also a person of ordinary creativity, not an automaton."). In the same vein, although an analysis of the teaching, suggestion, or motivation to combine elements from different prior art references is helpful, this Court's obviousness analysis requires an "expansive and flexible approach." *Kinetic Concepts, Inc. v. Smith & Nephew, Inc.*, 688 F.3d 1342, 1360 (Fed. Cir. 2012).

Finally, Watson, as the patent challenger, must prove obviousness by clear and convincing evidence.[4] *Tokai Corp. v. Easton Enterprises, Inc*., 632 F.3d 1358, 1367 (Fed. Cir.

[4] As stated above, during the prosecution of the '968 patent, the examiner considered and reviewed, *inter alia*, U.S. Patent No. 6,503,894 ("the '894 Dudley patent"), U.S. Patent Nos. 5,023,252 and 5,731,303 ("the Hsieh '252 patent and '303 patent"), and U.S. Patent No. 5,968,919 ("the '919 Samour patent"), as well as four out of five of the so-called "Bentley Disclosures." (DTX-011 at 373, 765–767; Trial Tr. 4.189:4-20, 4.190:13-22 (Barron); Trial Tr.

2011). Clear and convincing evidence is a higher burden of proof than preponderance of the evidence. *See Colorado v. New Mexico*, 467 U.S. 310, 316 (1984). To be clear and convincing, evidence must "place[ ] in the factfinder 'an abiding conviction that the truth of [the] factual contentions are highly probable.' " *Procter & Gamble*, 566 F.3d at 994 (quotation omitted).

Watson asserts that the claimed invention is invalid for obviousness because claim 3 of the ′607 patent would have been obvious to a POSA inasmuch as the scope and content of the prior art teaches all claimed elements. Auxilium responds that its claimed invention was not obvious because, *inter alia*, the prior art does not disclose the combination and concentrations of the components of claim 3, let alone that they would work in a testosterone gel for treating hypogonadism, and that a POSA would not have had a reasonable expectation of success in formulating a safe and effective transdermal pharmaceutical gel.

At trial, Watson, "like all those who seek to prove claims obvious, was required to show that 'the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains.'"

4.15:3-22 (Potts)). As such, the obviousness inquiry in this case is based largely on the same evidence presented to the PTO. To the extent Watson has an enhanced burden of overcoming deference to the PTO, the Court finds that Watson has met that burden. *Compare Tokai Corp. v. Easton Enterprises, Inc.*, 632 F.3d 1358, 1367 (Fed. Cir. 2011) ("[A]lthough the standard of proof does not depart from that of clear and convincing evidence, a party challenging validity shoulders an enhanced burden if the invalidity argument relies on the same prior art considered during examination by the . . . PTO.") *with Microsoft Corp. v. i4i Ltd. P'ship*, 131 S.Ct. 2238, 2250 (2011) ("Nothing in § 282's text suggests that Congress meant to depart from that understanding to enact a standard of proof that would rise and fall with the facts of each case. Indeed, had Congress intended to drop the heightened standard of proof where the evidence before the jury varied from that before the PTO—and thus to take the unusual and impractical step of enacting a variable standard of proof that must itself be adjudicated in each case—we assume it would have said so expressly.").

Galderma Labs., L.P. v. Tolmar, Inc., 737 F.3d 731, 737 (Fed. Cir. 2013) (citing 35 U.S.C. § 103).

Although Auxilium argues that the obviousness inquiry in this case should begin with the identification of a "reference composition" (or commercial embodiment) that a POSA would have used as a starting point during the relevant time period, this Court is not persuaded. The cases relied upon by Auxilium in support of this notion were cases involving chemical compounds. *See, e.g., Unigene Labs., Inc. v. Apotex, Inc.*, 655 F.3d 1352, 1361 (Fed. Cir. 2011) ("A prima facie case of obviousness in the chemical arts is often based on a known compound, called a "lead compound," which serves as a starting point for a person of ordinary skill developing the claimed invention."). This is not a chemical compound case—this case involves a pharmaceutical composition. Auxilium has failed to cite to any binding legal authority suggesting that the Court must use a reference composition framework in conducting an obviousness inquiry in a pharmaceutical composition case. *See generally Janssen Pharm., Inc. v. Watson Labs., Inc*., 2012 WL 3990221, at * 26 (D.N.J. 2012) ("In a chemical compound case, the obviousness inquiry begins before the prior art patent, and asks both whether there was a reason why the artisan would have selected the compound in the first patent as the lead compound, and then whether there was a reason to modify it.") (citing *Otsuka Pharm. Co. v. Sandoz, Inc*., 678 F.3d 1280, 1297 (Fed. Cir. 2012)). To the contrary, a more recent Federal Circuit case involving a pharmaceutical composition made clear that "[n]othing in the statute or our case law requires Tolmar to prove obviousness by starting with a prior art commercial embodiment and then providing motivation to alter that commercial embodiment." *Galderma*, 737 F.3d at 737.

Finally, while the party defending a patent may offer evidence of secondary considerations of nonobviousness, secondary considerations of nonobviousness may not overcome a strong prima facie case of obviousness. *Wyers v. Master Lock Co.*, 616 F.3d 1231, 1246 (Fed. Cir. 2010).

1. POSA

A person of ordinary skill in the art ("POSA") in this case would be a pharmaceutical formulation scientist, having at least a bachelor's degree and more likely an advanced degree, such as a master's or Ph.D. in pharmaceutical sciences or related sciences, such as chemistry or biology or biochemistry. A person with a master's degree or a bachelor's degree would typically have about ten years of formulation experience in transdermal or topical drug delivery, whereas less experience would be needed with somebody who had obtained a Ph.D. degree. (Trial Tr. 3.85:8-21 (Potts)); Trial Tr. 6.29:5-15 (Lane)).

2. Scope and Content of the Prior Art

In conducting the obviousness analysis, this Court views the claimed invention in light of the art that existed at the time the invention was made. *See* 35 U.S.C. § 103(a); *Uniroyal, Inc. v. Rudkin-Wiley Corp.*, 837 F.2d 1044, 1050–51 (Fed. Cir. 1988). "Prior art has been defined as follows: '[t]he existing state of knowledge in a particular art at the time an invention is made. It includes the issued patents * * *, publications, and all other knowledge deemed to be common thereto such as trade skills, trade practices, and the like,' " available a year or more before the patent filing date." *Trio Process Corp. v. L. Goldstein's Sons, Inc*., 461 F.2d 66, 69 n. 3 (3d Cir. 1972) (quoting A. Smith, PATENT LAW, CASES, COMMENTS AND MATERIALS 2 (1964)).

Section § 102(b) provides, in relevant part, that an invention is not patentable if it was "described in a printed publication" more than one year prior to the filing date of the application from which the patent issued. 35 U.S.C. § 102(b). A prior art reference cannot constitute a "printed publication" under § 102(b) if it has not been made "publicly accessible." *In re Klopfenstein*, 380 F.3d 1345, 1348 (Fed. Cir. 2004). Thus, as stated above, the critical date for the Court's analysis of prior art (under 35 U.S.C. § 102(b)) to the asserted patents is April 19, 2001, and this Court considers all the teachings in the prior art in the obviousness determination, "including that which might lead away from the claimed invention." *In re Dow Chem. Co*., 837 F.2d 469, 473 (Fed. Cir. 1988).

The Court has considered numerous prior art references, the most relevant of which are: AndroGel® and the '894 "Dudley" Patent;[5] the '919 (Samour) patent;[6] the Mak Reference; [7] the '252 and '303 (Hsieh) patents;[8] the Bentley Disclosures;[9] and the Gauthier Reference.[10] Whether

[5] The '894 Dudley Patent is § 102(e) prior art. AndroGel® is § 102(b) prior art.

[6] The '919 Samour patent issued on October 19, 1999 and is thus 102(b) prior art.

[7] The '041 Mak Reference was published on May 20, 1999 and is thus § 102(b) prior art.

[8] The '252 and '303 patents are prior art under 35 U.S.C. § 102(b).

[9] Each of the Bentley Disclosures was published prior to April 19, 2001; thus, the Bentley Disclosures are § 102(b) prior art. To the extent Auxilium argues that the Bentley Disclosures are not § 102(b) prior art because they are not scientific documents (i.e., the types of documents that a POSA would turn to in order to inform the development of transdermal testosterone gels) and/or that such disclosures do not constitute "analogous" prior art, Auxilium cites to no legal authority in support of its position. To the contrary, the Federal Circuit has recognized that press releases can constitute prior art for purposes of obviousness. *See, e.g., In re Morsa*, 713 F.3d 104, 111-12 (Fed. Cir. 2013) (affirming obviousness rejection of patent claims over single prior art press release). Moreover, the Court finds that Watson has established, by clear and convincing evidence, that the Bentley Disclosures—which disclosed, in pertinent part, that clinical studies had been undertaken by Auxilium vis-à-vis its topical testosterone gel formulation containing CPE-215, *and* that a Phase III study had recently commenced—would have been significant to the POSA and thus constitutes analogous prior art because it was "obviously . . . promising for the drug" (Trial Tr. 6.148:16-23 (Lane)), and demonstrates to the

or not Dr. Hsieh's Permeation Studies constitute prior art for purposes of an obviousness analysis is hotly disputed. Although Dr. Hsieh's Permeation Studies (containing his testosterone gel formulations) were not publicly accessible, Watson maintains that, for purposes of obviousness, they are prior art under the § 102(b) on-sale bar. The Court will address whether the Permeation Studies constitute § 102(b) prior art below.

The Court begins by noting that there is no bright line distinction between a topical gel and a transdermal gel. (Trial Tr. 3.90:1-19 (Potts)). Both seek to penetrate the rate-limiting outermost layer of the skin, the stratum corneum. Transdermal formulations aim to deliver a drug through the skin and into blood circulation. In contrast, topical formulations aim to deliver a drug to the skin itself with minimal uptake of the drug into the blood supply (*i.e.*, minimal systemic uptake). The critical factor is the amount of drug in the gel and the length of time for which it is applied – the more drug in the gel and the longer it is applied, the more likely it will reach the bloodstream and have a systemic effect. (Trial Tr. 3.90:20-3.91:19 (Potts)).

It was well known by April 2001 that testosterone was suitable for transdermal delivery. (Trial Tr. 3.88:17-3.89:5, 3.89:11-16 (Potts); Trial Tr. 6.29:16-6.30:2 (Lane)). By that point in time, there was one FDA-approved transdermal testosterone gel formulation on the market—

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public that a testosterone gel with CPE-215 had already been shown to be effective in humans, and was safe and stable enough to be progressed even further. (Trial Tr. 6.150:16-6.151:1 (Lane); Trial Tr. 3.121-3.127 (Potts)). The Court finds particularly convincing the testimony by Dr. Potts that, in his career as a pharmaceutical formulator, he has searched public relations documents, securities documents, and trademark records "for information about development of competitive products in order to inform the development and strategy, and all of the aspects of developing a product." (Trial Tr. 3.118:16-3.119:10, 3.120:14- 21 (Potts)). Evidence introduced at trial also shows that Bentley provided four out of five of the Bentley Disclosures to the PTO for its consideration during the prosecution of the '968 patent, a parent of the application that issued as the '607 patent. (DTX-011 at 373, 765–767; Trial Tr. 4.189:4-20, 4.190:13-22 (Barron); Trial Tr. 4.15:3-22 (Potts)). For all of these reasons, Auxilium's position that the Bentley Disclosures are not § 102(b) prior art is rejected.

[10] Dr. Gauthier's Abstract and Thesis, which were published in June 2000, are § 102(b) prior art.

AndroGel®. Thus, by April 2001, a POSA would have been motivated to develop a transdermal testosterone gel that would be better than or as good as AndroGel®.

a. Testosterone References

i. AndroGel® and the '894 "Dudley" Patent

U.S. Patent No. 6,503,894, issued to Robert Dudley et al. ("the '894 Dudley Patent") from a patent application filed on August 30, 2000, is entitled "Pharmaceutical Composition and Method for Treating Hypogonadism." The '894 Dudley patent discloses a testosterone transdermal gel and a method for treating hypogonadism. AndroGel®, the only testosterone gel example contained in the '894 Dudley patent, is disclosed in Table 5 therein. AndroGel® was approved by the FDA in February 2000 and was commercially available in the United States prior to April 2001. AndroGel® was the most common form of treatment for low testosterone in April 2001.

The AndroGel® composition comprises: 1.0% testosterone, 0.9% carbopol 980, 0.5% isopropyl myristate (a permeation enhancer), 4.72% 0.1 N NaOH, 72.5% ethanol, and water. (DTX-029 at Table 5). The '894 Dudley patent also discloses that the following ingredients can be used in the claimed testosterone gels: propylene glycol, glycerin, and polyethylene glycol. (DTX-029 at col. 12, ll. 39:59; Trial Tr. 6.109:9-6.110:1 (Lane)).

ii. The '919 Patent, the "Samour Patent"

The U.S. Patent No. 5,968,919 ("the '919 Samour patent") entitled "Hormone Replacement Therapy Drug Formulations for Topical Application to the Skin" lists Dr. Carlos Samour, Scott Krauser, and Robert Gyurik as named inventors. The '919 Samour patent teaches "stable topical compositions effective for the transdermal application of testosterone, estradiol, or other hormone compounds by the application of the compositions to the skin." (DTX-031 at

col. 4, ll. 30-34, Trial Tr. 3.102:24-3.103:4 (Potts)). The '919 Samour patent claims a gel composition containing about 0.1-10% testosterone, about 2-20% of a permeation enhancer, 0-25% propylene glycol, 35-75% ethanol or isopropanol, 0-35% water, and 0-4% of a thickening agent. (DTX-031 at claim 1). Claim 1, the broadest claim of the '919 Samour patent, claims, *inter alia*, about 2-20% of the SEPA® permeation enhancer. Example 7 is the only example in the '919 Samour patent of a complete testosterone gel formulation. (DTX-031 at 12).

iii. The '041 Publication, the "Mak Reference"

The World Intellectual Property Organization International Application No. WO 99/24041, ("the '041 Mak Reference") entitled "Penetration Enhancing and Irritation Reducing Systems," lists Vivien Mak as the inventor. (DTX-049 at 1). The '041 Mak Reference was published on May 20, 1999. The '041 Mak Reference discloses permeation-enhanced topical testosterone gel formulations including the following composition: testosterone, oleic acid (permeation enhancer), Carbopol 1342 (thickening agent), ethanol, isopropyl alcohol, propylene glycol, skin irritation reducing agent (i.e., glycerol), triethanolamine, and water. (DTX-049 at Table 4).

iv. Testosterone Gels Generally

The testosterone gels taught in the prior art, including AndroGel®, the '894 Dudley Patent, the '919 Samour Patent, and the '041 Mak Reference, have several common ingredients. All have testosterone, a permeation enhancer, a thickening agent, and several excipients that were well known to the POSA, i.e., ethanol, propylene glycol, polyethylene glycol, and glycerin. (Trial Tr. 3.107:15-3.108:11 (Potts)). The prior art demonstrated that testosterone is compatible in a gel with these ingredients. (Trial Tr. 3.108:12-16 (Potts)).

By April 2001, a large number of fatty acids and fatty acid derivatives, as described in the '894 Dudley patent and the '041 Mak Reference, were recognized as potential permeation enhancers and had attained GRAS status (*i.e.,* were generally recognized as safe). (Trial Tr. 4.43:13-19, 4.44:4-13 (Potts)). Macrocyclic enhancers, one of which is CPE-215, are chemically different from fatty acids and fatty acid derivatives. With the exception of Testim®, AndroGel® and all follow gel products use fatty acid or fatty acid derivative enhancers that are described in the '894 Dudley patent or derived from the enhancers described in the '894 Dudley patent. Testim® is the only pharmaceutical product on the market to date that uses CPE-215 (a macrocyclic enhancer) as a permeation enhancer, even though the '252 patent (discussed below) expired in 2008.

b. CPE-215 References

i. Bentley Disclosures

The "Bentley Disclosures," discussed in greater detail below, are a series of press releases and financial statements that were made public by Bentley prior to April 19, 2001. (DTX-038, DTX-039, DTX-040, DTX-041; Trial Tr. 6.101:12-15 (Lane)).

On June 6, 2000, Bentley Pharmaceuticals issued a press release entitled "Bentley Pharmaceuticals Announces Research and Licensing Agreements for its Topical Testosterone Gel Formulation." (DTX-038). In the press release, Bentley announced that it had entered into an agreement with Auxilium A2, Inc. to license a new topical gel formulation of testosterone in combination with its permeation facilitator, CPE-215. The June 6, 2000 press release quoted James R. Murphy, chairman and CEO of Bentley:

> We are pleased to announce this step toward our first license for a product based upon our CPE-215 permeation enhancement technologies for improving the absorption of a wide range of therapeutic agents. Our initial evaluation of this product indicates

> that we have an impressive formulation that enhances the topical absorption of testosterone over non-enhanced formulations, which will facilitate the use of a small quantity of fast drying gel. Our CPE-215 technology combined with testosterone will provide patients the convenience of a self-administered, simple topical application rather than a more aggressive therapy involving injections. . . . It is believed as much as 25 percent of the male population over the age of 50 have low levels of testosterone and approximately 5 million men suffer hypogonadism . . . Although the worldwide market for testosterone products during 1999 approached $150 million, as baby-boomers approach middle age and more attention becomes focused on male hormonal deficiencies, the market could evolve to a very sizeable level.

(DTX 38).

On December 18, 2000, Bentley issued another press release entitled "Bentley Pharmaceuticals Announces License Agreement for its Topical Testosterone Gel Formulation; License is First for CPE-215 Permeation Technology." (DTX-039). This press release is listed on the face of the '894 Dudley patent under "Other Publications." (DTX-029 at 2). In the December 18, 2000 press release, Bentley announced "that the license agreement with Auxilium A2 Inc. for a new topical gel formulation of testosterone in combination with Bentley's permeation facilitator CPE-215®, has become effective." (DTX-39). Mr. Murphy is quoted again: "We are pleased that Auxilium has completed its due diligence phase and is now moving rapidly to develop a commercial product. Our CPE-215® technology combined with testosterone should provide patients the convenience of a self-administered, improved absorption topical application." (*Id.*). The PTO records showed that CPE-215 was the trademark name for cyclopentadecanolide. (DTX-037; Trial Tr. 3.120:3-13 (Potts)). Dr. Potts testified that, in his career as a pharmaceutical formulator, he has searched public relations documents, securities documents, and trademark records "for information about development of competitive products in order to inform the development and strategy, and all of the aspects of developing a product."

(Trial Tr. 3.118:16-3.119:10, 3.120:14-21 (Potts)). He could not, however, recall a specific instance when he used such information to make a decision about what components to put into a formulation. (Trial Tr. 4.20:13-20 (Potts)).

In Bentley's Annual Report, filed with the Securities and Exchange Commission on April 2, 2001, Bentley stated that "Auxilium is applying [CPE-215] to topical gel formulation of testosterone. Clinical studies have been undertaken by Auxilium and a Phase III study has recently commenced." (DTX-041 at 9; Trial Tr. 3.120:22-3.121:15 (Potts)).

During prosecution of the '968 patent, the examiner considered four out of five of the so-called "Bentley Disclosures." (DTX-011 at 373, 765-767; Trial Tr. 4.189:4-20, 4.190:13-22 (Barron); Trial Tr. 4.12:7-22 (Potts)).

The Bentley Disclosures taught the successful use of CPE-215 in a testosterone transdermal gel. (Trial Tr. 6.101:12-15 (Lane)).

ii. Other Press Releases

Cellegy — another pharmaceutical company —announced Phase III clinical trials of its transdermal testosterone gel, using oleic acid (one of the enhancers disclosed in the '894 Dudley patent) on March 29, 2000—a year ahead of the Bentley Disclosures.

In April 2000, MacroChem announced that the SEPA®—its own proprietary permeation enhancer—exhibited clear superiority compared to CPE-215 when used with testosterone. (Trial Tr. 4.63:17-4.64:24 (Potts)).

iii. The Hsieh Patents

On June 11, 1991, Dr. Hsieh was issued a patent, U.S. Patent No. 5,023,252 ("the '252 patent"), entitled "Transdermal and Trans-Membrane Delivery of Drugs." (DTX-027). On March 24, 1998, Dr. Hsieh received another patent, U.S. Patent No. 5,731,303 ("the '303

patent"), entitled "Transdermal and Trans-Membrane Delivery Compositions." (DTX-028). The '303 patent is a continuation in part of the '252 patent. The '252 and '303 patents were both before the PTO during prosecution of the '607 patent.

The '252 and '303 patent are directed to enhancing the permeation of drugs across the skin and other bodily membranes by applying a composition comprising a permeation enhancer, including among others CPE-215 (cyclopentadecanolide). (DTX-027 at abstract, claims 1-53; DTX-028 at abstract, claims 1-7). The data in Table 5 of the '303 patent shows that CPE-215 substantially outperformed other Hsieh enhancers in a Franz cell test measuring the permeation rate of hydrocortisone through hairless mouse skin. (DTX-028 at table 5; Trial Tr. 3.128:7-3.129:16 (Potts)). Dr. Potts and Dr. Lane both agreed that CPE-215 was the best performing—by far—of the permeation enhancers discussed in Dr. Hsieh's patents. (Trial Tr. 3.128:7-3.129:16 (Potts); 6.90:12-17 (Lane)).

The '252 and '303 patents teach the use of CPE-215 to enhance the transdermal delivery of "steroidal hormones," i.e., the class of therapeutic agents encompassing testosterone. (DTX-027 at col. 14:42-60; DTX-028 at col. 13:65-14:15, 22:42-43; Trial Tr. 6.103:16-6.104:24 (Lane); Trial Tr. 3.98:21:3.100:2 (Potts)).

In addition, the '303 patent teaches that CPE-215 can be used in a pharmaceutical composition in concentrations ranging between 0.1 – 30 wt %. (DTX-028 at col. 23, ll. 19-27). Example 25 of the '303 patent discloses an antifungal topical composition "in the form of a gel." The gel comprises 1.0% clotrimazole (active ingredient) 4.0% CPE-215 (penetration enhancer), 1.5% Carbomer 940 (thickening agent), 30% ethanol, 15% glycerin, and 30% propylene glycol. (DTX-028 at Example 25, Trial Tr. 3.130:16-3.131:7 (Potts); Trial Tr. 6.106:5-18 (Lane)).

iv. The Permeation Studies

As early as 1994, Dr. Dean Hsieh developed several testosterone gels containing CPE-215, ethanol, propylene glycol, and glycerin. (DTX-147 at 3-4, 25; Trial Tr. 6.157:10-6.161:5 (Lane)). Dr. Hsieh had permeation testing conducted on these testosterone gels and they were shown to work. (DTX-147 at 2-29). Dr. Hsieh never identified any stability problem with his testosterone gels.

As stated above, although Dr. Hsieh's Permeation Studies (containing his testosterone gel formulations) were not publicly accessible during the relevant time period, Watson maintains that, for purposes of obviousness, they are prior art under the § 102(b) on-sale bar. "The on-sale bar applies when two conditions are satisfied before the critical date: (1) the claimed invention must be the subject of a commercial offer for sale; and (2) the invention must be ready for patenting." *Hamilton Beach Brands, Inc. v. Sunbeam Prods., Inc.*, 726 F.3d 1370, 1374 (Fed. Cir. 2013). "An invention is 'ready for patenting' when prior to the critical date: (1) the invention is reduced to practice; or (2) the invention is depicted in drawings or described in writings of sufficient nature to enable a person of ordinary skill in the art to practice the invention." *Hamilton Beach Brands*, 726 F.3d at 1375. "[I]n some cases a proposed sale of an inventor's business may amount to little more than the sale of one or more specific inventions or machines of which they are a part. In such circumstances the inventions themselves would be on sale within the literal meaning of section 102(b)." *Micro-Magnetic Indus., Inc. v. Advance Automatic Sales Co., Inc.*, 488 F.2d 771, 772-773 (9th Cir. 1973). As such, this Court has previously held that the question in the instant matter is whether the transfer of assets from Conrex to Bentley constituted "little more than the sale of one or more specific inventions." *Micro-Magnetic*, 488 F.2d at 772-73.

Based on the reasons that follow, the Court concludes that Watson did not establish by clear and convincing evidence that the sale of the pharmaceutical side of Conrex (which *included* the Permeation Studies) qualifies as prior art under the § 102(b) on-sale bar.

The Asset Purchase Agreement entered into by the parties (effective December 31, 1998), defined "Assets" broadly as: (1) Technology; (2) Business Information; (3) Patents; (4) "all Contracts relating to the Patents and Technology that are listed . . . [in] Disclosure Schedule"; (5) all Licenses; (6) "lists of suppliers and supply agreements, if any"; and (7) "all batch records in existence as of . . . Closing Date." (DTX-45). Mrs. Hsieh testified that "[e]verything [was] transferred to Bentley" and "[a]ll the information, whatever happened to Conrex [was] given to Bentley." (Trial Tr. 1.172:10-1.174:11 (Hsieh)). Bentley's then-CEO, Mr. Murphy, agreed that Bentley entered into the Asset Purchase Agreement "to purchase all [of Conrex's] drug-related activity[,] the entire drug side of Conrex." (Trial Tr. 1.196:5-10 (Murphy)). In light of this evidence, and notwithstanding the fact that the materials actually transferred from Conrex to Bentley comprised only 2-5 filing cabinet boxes, the Court finds that Watson did not establish by clear and convincing evidence that Dr. Hsieh's testosterone gel formulation (which was included in the Permeation Studies) was, itself, the subject of a commercial offer for sale under § 102.[11]

[11] As such, the Court need not determine whether Dr. Hsieh's testosterone gel formulations were "ready for patenting." *See generally Hamilton Beach Brands*, 726 F.3d at 1375. Even assuming, *arguendo*, that Watson *had* established that Dr. Hsieh's testosterone gel formulation(s) was the subject of a commercial offer for sale under § 102, the Court would in any event conclude that Watson did not establish, by clear and convincing evidence, that Dr. Hsieh's testosterone gel formulations were "ready for patenting." The evidence established that, at most, Dr. Hsieh was in the process of trying to commercialize his formulation(s) when he died unexpectedly. Evidence in the record confirms that Dr. Hsieh's formulations, although containing the key ingredients of what would later become a pharmaceutical composition—an androgen, a Hsieh enhancer, and a thickening agent—had not yet been tested on humans; thus, there is no indication that it would work for its intended purpose of treating hypogonadism in adult males, safely and effectively. (Trial Tr. 3.211:25-3.212:13 (Potts). *See, e.g.*, *In re*

This conclusion is corroborated by the fact that Mr. Gyurik spent a full year working on a number of *other* projects—including antifungal clotrimazole topical delivery formulations and insulin intranasal delivery formulations—based on materials Bentley had acquired from Conrex *before* he even began working with testosterone formulations. (Trial Tr. 2.25:10-18, 2.27:19-23, 2.29:11-14, 2.29:25-2.31:18, 2.34:9-23, 2.35:5-11, 2.35:23-2.36:3 (Gyurik). As such, the Court declines to consider Dr. Hsieh's Permeation Studies (and the testosterone gel formulations contained therein) as prior art under the § 102(b) on-sale bar.

v. Gauthier Reference

Between 1997 and 2000, Ph.D. student Eric Gauthier compared a permeation enhancer called "SEPA®" against two Hsieh enhancers (CPE-215 and cyclopentadecanone) in enhancing testosterone permeation over the course of 24 hours. Gauthier did not conduct research on testosterone gels; rather, he conducted his research on testosterone solutions. Gauthier was employed by MacroChem at the time of his work. SEPA® was MacroChem's proprietary permeation enhancer. Gauthier interpreted the 8 hour data as showing that SEPA® exhibited "clear superiority" over the other permeation enhancers tested—including CPE-215.

In discussing how a transdermal gel is used, Dr. Lane explained that "a transdermal gel is applied by the patient onto the skin. The drug needs to move out of that gel and be released from it all the way through the different layers of the skin until it accesses the blood supply in the dermis. Once it is in the blood supply, it is carried away to its target site." (Trial Tr. 1.119:19-25 (Lane)). The amount of drug "that gets into the dermis is important" for a transdermal product,

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Omeprazole Patent Litig., 536 F.3d 1361, 1373 (Fed. Cir. 2008) (finding pharmaceutical formulation not ready for patenting prior to clinical trials, and noting that "[t]he existence of the formulation, however, does not establish that the Astra scientists had determined that the invention would work for its intended purpose.").

because as Dr. Lane testified, if a drug reaches the dermis layer "it can enter the blood vessels for purposes of systemic circulation." (Trial Tr. 6.135:15-6.136:4; 6.139:6-17 (Lane)). Despite having measured the amount of testosterone that penetrated into each of the epidermis *and* dermis layers of the skin, Gauthier only reported his data for the epidermis.

Moreover, in an abstract published for a scientific meeting, Gauthier provided only the data collected after 8 hours even though he ran his experiment and collected data for 24 hours. (DTX-047, Trial Tr. 6.67:9-13 (Lane)). As stated above, Gauthier interpreted the 8 hour data as showing that SEPA® exhibited "clear superiority" over the other permeation enhancers tested—including CPE-215. (DTX-047). The 24 hour data, by contrast, showed that "the enhancers, *all* enhancers [including CPE-215], increase the amount of drug recovered from the skin following 24 hours exposure." (Trial Tr. 3.167:4-13 (Potts)) (emphasis added).

3. Differences Between Prior Art and Claimed Invention

Prior art taught that CPE-215 could be used in a testosterone gel. In particular, the Bentley Disclosures teach CPE-215 in a testosterone gel (Trial Tr. 6.101:12-15 (Lane)), and the '252 and '303 patents teach CPE-215 in compositions containing steroidal hormones, a term that includes testosterone. (Trial Tr. 6.103:16-6.104:24 (Lane), Trial Tr. 3.98:21-3.100:2 (Potts)).

a. Ingredients

The ingredients used in the claimed invention were disclosed in the prior art to work in both testosterone gels and gels containing CPE-215. (Trial Tr. 6.113:15-6.114:2, 6.119:20-6.120:14, 6.121:12-6.123:4 (Lane)). In particular, Dr. Lane testified that the '303 patent taught a gel containing CPE-215, a thickening agent, ethanol, glycerin, and propylene glycol, and Dr. Potts agreed. (Trial Tr. 6.105:23-6.106:18 (Lane); Trial Tr. 3.152:24-3.153:7, 3.154:18-25 (Potts)). Dr. Lane admitted the '894 Dudley patent teaches a testosterone gel containing a

thickening agent, a permeation enhancer, ethanol, propylene glycol, glycerin, and polyethelene glycol (DTX-029 at col. 13, ll. 36-43, col. 12, ll. 39:59; Trial Tr. 6.109:9-6.110:1 (Lane)). Dr. Lane agreed that the '919 Samour patent teaches a testosterone gel containing a permeation enhancer, propylene glycol, ethanol, thickening agent, and glycerin. (DTX-031 at claim 1; Trial Tr. 6.108:7-6.109:8 (Lane)).

In light of AndroGel®, the '919 patent and the Mak Reference, the Court concludes that by 2001, it was well-established in the art that testosterone could penetrate the skin and therefore could be used in gel formulations.

In light of Dr. Hsieh's patents and the Bentley Disclosures, the Court further concludes that the prior art disclosed the use of CPE-215 as a permeation enhancer that could be used with testosterone in a gel. In particular, the Court finds that Dr. Hsieh's '252 and '303 patents disclose Dr. Hsieh's "Hsieh enhancers," show that CPE-215 was the best of those enhancers, and teach the use of CPE-215 to enhance the transdermal delivery of "steroidal hormones." As discussed above, testosterone is an example of a male steroidal hormone. *See* Trial Tr. 6.103:16-6.104:24 (Lane); Trial Tr. 3.98:21:3.100:2 (Potts)).

As to the excipients, the Court finds that a POSA would have known about the short list of well known, regularly used, and FDA-approved pharmaceutical excipients in developing the claimed testosterone gel. As discussed above, Dr. Gyurik's testimony at trial confirmed that there were a finite number of options available to the POSA to include in a pharmaceutical composition. *See, e.g., KSR*, 550 U.S. at 421 ("When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill

and common sense."). In particular, Mr. Gyurik testified that "there is a very short list of components that are suitable for pharmaceutical formulations given in the national compendiary." (Trial Tr. 2.122:8-2.123:11 (Gyurik)). In other words, there is a finite number of options that have been approved by the FDA which are readily available to a POSA in developing a composition. (Trial Tr. 2.122:8-2.123:11 (Gyurik)). This short list of excipients—which Mr. Gyurik estimated to be a "couple" pages long—are used by an ordinary formulator "over and over again in a similar way." (Trial Tr. 2.122:8-2.123:11 (Gyurik)).

Therefore, based on the prior art, discussed above, the Court concludes that the following excipients are components from the formulator's proverbial "toolbox" that would allow a POSA to formulate a topical gel that includes testosterone and a permeation enhancer: ethanol, propylene glycol, glycerin, and polyethylene glycol. *See* Trial Tr. 3:107-1:1-13; 3:157:7-3.158:6 (Potts). For example, the claimed excipient polyethylene glycol ("PEG")—which was known in the art to have multiple potential functions in specific formulations, e.g., a crystallization inhibitor, a lubricant, a skin irritation reducing agent—was among the "finite number of options" that a POSA would know to use in a pharmaceutical composition. (Trial Tr. 3.157:7-3:158:6 (Potts); Trial Tr. 2.169:13-20 (Gyurik)).

b. Amount

Claim 3 of the '607 patent recites:

> 3. A method for maintaining a therapeutically effective concentration of testosterone in the blood serum of a male for treating hypogonadism which comprises transdermally delivering to the male by applying to the skin a composition which is in the form of a topical gel, which has a viscosity of about 500 to about 20,000 cps and a pH of about 3 to 9, and comprises:
> (A) about 0.1 to about 5 wt. % of testosterone;
> (B) about 0.5 to about 15 wt. % of oxacyclohexadecan-2-one;
> (C) about 0.1 to about 10 wt. % of a thickening agent;
> (D) a mixture of solvents which include:

> (i) about 60 to about 75 wt. % of ethanol or isopropanol; and
> (ii) propylene glycol and glycerin as co-solvents;
> and further comprising polyethylene glycol, wherein the polyethylene glycol ranges from about 0.001 to about 5 wt. %.

(DTX-004). Based on the reasons that follow, the Court finds that not only were the claimed ingredients taught in prior art, but their claimed concentration ranges also overlap with and were taught in the prior art.

The Court begins by noting that the asserted claim covers a method for treating low testosterone and compositions that have certain pH and viscosity ranges. Dr. Potts testified—and this Court agrees—that this method, as a general matter, would have been obvious to the POSA by virtue of AndroGel® and the Bentley Disclosures. He also testified that these particular limitations—as to viscosity and pH—were known and would have been obvious to the POSA. (Trial Tr. 3.148:15-3.150:22 (Potts); DTX-031 at 10). In particular, Dr. Potts testified that neutral is the preferred pH—with a seven representing neutrality—inasmuch as a very high or low pH would be skin irritating. This was also taught by the '919 Samour patent. (DTX 31 at 10) ("Generally, neutral to slightly basic pH's are preferred."). As to viscosity, Dr. Potts testified that the claimed range—of about 500 to about 20,000 cps—was a "very broad range." (Trial Tr. 3.148:15-3.150:22 (Potts)). This Court agrees with Dr. Potts that the broad range of viscosity claimed in the '607 patent was generally known in the art and substantially overlaps with the ranges disclosed in the '919 (Samour) patent (teaching the lower end of the range)[12] and the '958

[12] (Trial Tr. 4.69:70:15 (Potts) (citing DTX 31 at 10).

(Kochinke) patent[13] (teaching the middle of the range, 100 to 10,000 cps, for gel component of transdermal device). (DTX 31 at 10; DTX 32 at 17); (Trial Tr. 4.81:1-13 (Potts)). *See, e.g., In re Geisler*, 116 F.3d 1465, 1470 (Fed. Cir. 1997) ("[I]t is not inventive to discover the optimum or workable ranges by routine experimentation. Only if the 'results of optimizing a variable' are 'unexpectedly good' can a patent be obtained for the claimed critical range."); *see generally Beckson Marine*, 292 F.3d at 727 ("[O]obviousness does not require the prior art to reach expressly each limitation exactly."); *Hartness Int'l, Inc. v. Simplimatic Eng'g Co.*, 819 F.2d 1100, 1108 (Fed. Cir. 1987).

Turning back to the claimed ingredients, the '894 Dudley patent teaches a 0.1%-10% testosterone gel containing 0.1-5.0% thickening agent, 30.0-98.0% ethanol, propylene glycol, glycerin, and polyethelene glycol (DTX-029 at col. 13, ll. 36-43, col. 12, ll. 39:59; Trial Tr. 6.109:9-6.110:1, 6.121:12-6.123:4 (Lane); Trial Tr. 3.155:1-22 (Potts)). Dr. Lane also agreed that the '919 Samour patent teaches a testosterone gel containing 0-25% propylene glycol, 35-75% ethanol, 0-4% thickening agent, and 0.1-5% glycerin. (DTX- 031 at claim 1, col. 8:48-53, Trial Tr. 6.108:7-6.109:8, 6.121:12-6.123:4, 6.167:5-6.170:25 (Lane); Trial Tr. 3.155:23-3.157:5 (Potts)). Moreover, the '303 patent teaches that CPE-215 can be used in a pharmaceutical composition in concentrations ranging between 0.1–30 wt %, containing, among other things, 1.5% of a thickening agent. (DTX-028 at col. 23, ll. 19-27; Trial Tr. 3.152:13-3.152:19 (Potts)). As such, the claimed concentration ranges of testosterone, CPE-215 and ethanol were precisely disclosed in the prior art.

[13] U.S. Patent No. 5,613,958 (the '958 patent) (describing a transdermal delivery system for the modulated administration of drugs) issued on March 25, 1997 and is thus § 102(b) prior art. (DTX 32).

As to the claimed range for the thickening agent (about 0.1 to about 10 wt. %), although the *higher* end of the claimed range was not necessarily taught in the prior art, the Court finds that the claimed range was generally known in the art and substantially overlaps with the ranges disclosed in the '894 Dudley patent (0.1-5.0%), '919 Samour patent (0-4%) and in Example 25 of the '303 Hsieh patent (1.5%). Moreover, the '919 Samour patent specifically taught that "the amount of the thickening agent is not particularly critical and can be selected to provide the desired product consistency or viscosity." (DTX 31 at 10). As stated above, it is "not inventive to discover the optimum or workable ranges by routine experimentation." *In re Geisler*, 116 F.3d at 1470.

As to the claimed ingredient of polyethylene glycol ("PEG"), although the claimed *amount* of PEG was not disclosed in prior art, Dr. Gyurik himself testified that "it was generally known about PEG-1000 and tackiness." Trial Tr. 2.169:13-170:4 (Gyurik)). Dr. Potts testified that PEG is "absolutely a major component of the formulator's toolbox" and that it is precisely the role of the formulator to "tweak the amounts . . . in order to achieve an optimal formulation." (Tr. 3.158:3-3.159: 8 (Potts)). As such, the Court agrees with Dr. Potts that it would have been obvious to the POSA to use the "vanishingly small" amount of PEG claimed to be a crystallization inhibitor, co-solvent, or to reduce the tackiness of the gel. (Trial Tr. 3.157:7-3:159:8 (Potts); Trial Tr. 2.169:13-20 (Gyurik)). *See, e.g., Pfizer, Inc. v. Apotex, Inc*., 480 F.3d 1348, 1368 (Fed. Cir. 2007) ("[T]he discovery of an optimum value of a variable in a known process is usually obvious.").

4. The Motivation to Combine the Prior Art

In April 2001, the testosterone replacement therapy market was expected to grow significantly, to the tune of hundreds of millions of dollars. (DTX-038). At that time, a POSA

would have been motivated to develop a transdermal testosterone gel that would be better than, or as good as, AndroGel®--which had been approved by the FDA in 2000 and was, as of April 2001, the only FDA-approved transdermal gel formulation for any active ingredient, not just testosterone. (Trial Tr. 3.202:12-15 (Potts)).

The permeation enhancer in a transdermal gel is a "key" and an "important" ingredient in a testosterone transdermal gel. (Trial Tr. 2.203:6-9 (Gyurik)). Certainly, the POSA would have been motivated to combine the prior art to develop a testosterone gel with a strong permeation enhancer. Although the ability of a permeation enhancer to enhance permeation of one active ingredient is not necessarily indicative of the ability of the same enhancer to enhance permeation of another active ingredient, the POSA would have understood, based on data in the '252 and '303 patents, that CPE-215 was a strong permeation enhancer that could be used in a gel and with steroidal hormones—including testosterone. (Trial Tr. 3.126:19-3.131:13 (Potts)). By contrast, Mr. Gyurik testified that AndroGel® "has a very weak lipohilic permeation enhancer"—namely, isopropyl myristate. (Trial Tr. 3.70:10-23 (Gyurik)).

As discussed above, the Bentley Disclosures describe a testosterone gel containing CPE-215 having entered a Phase III clinical trial. (Trial Tr. 3.121:1-15 (Potts)); (DTX 38). A Phase III trial is the last clinical trial conducted before a drug is submitted for final FDA approval. (Trial Tr. 3.121:17-23 (Potts)). It is complex in design, involves a large patient population with multiple trial locations, and generally marks a significant and very expensive milestone in drug development. (Trial Tr. 3.121:17-3.122:3 (Potts)). A Phase III trial would have been significant to the POSA because "obviously that is promising for the drug." (Trial Tr. 6.148:16-23 (Lane)). The commencement of a Phase III trial also demonstrated that a testosterone gel with CPE-215 had already been shown to be effective in humans, and was safe and stable enough to be

progressed even further. (Trial Tr. 6.150:16-6.151:1 (Lane); Trial Tr. 3.121-3.127 (Potts)). Therefore, the Court concludes that a POSA would be motivated to combine CPE-215 with a testosterone gel based on the teachings in the Bentley Disclosures and the '252 and '303 patents. (Trial Tr. 3.126:12-3.132:1 (Potts)). Put differently, the Court finds that the Bentley Disclosures would have provided a POSA the motivation to include a Hsieh enhancer in the permeation-enhanced testosterone gel disclosed in the Dudley patent.

Although a POSA could not necessarily predict whether a given formulation would be stable without testing it, this Court finds that a POSA would have been motivated to use the excipients that were known to work with CPE-215 and testosterone gels. Thus, based on Example 25 in the '303 patent, a POSA would have known that CPE-215 was known to work with a thickening agent, ethanol, propylene glycol, and glycerin. Based on the '894 Dudley patent and the '919 patent, a POSA would have understood that the claimed concentration ranges of ethanol, propylene glycol, glycerin, and polyethylene glycol were known to work with testosterone gels. Moreover, as discussed above, the POSA would have been working with the "very short list" of excipients regularly used in compositions and approved by FDA, including ethanol, propylene glycol, glycerin, and polyethylene glycol (PEG).

a. The Gauthier Reference and MachroChem

Having carefully considered Gauthier's research, MachroChem's corresponding announcement regarding the superiority of its SEPA® permeation enhancer, and the witnesses testimony regarding same, the Court concludes that Gauthier's research does not teach away from the use of CPE-215 in a testosterone gel. To the contrary, the Court finds that Gauthier's research—which tested solutions, not gels—confirmed overall interest in CPE-215 during the relevant period. That SEPA® may have outperformed CPE-215 in the 8 hour data, does not

negate the fact that the 24 hour data indicated that "the enhancers, *all* enhancers [including CPE-215], increase the amount of drug recovered from the skin following 24 hours exposure." (Trial Tr. 3.167:4-13 (Potts)) (emphasis added). Thus, the Court agrees with Dr. Potts that the data in the Gauthier thesis still showed some positive results vis-à-vis CPE-215 and thus did not teach away from the use of CPE-215 in a testosterone gel. (Trial Tr. 4:51:25-4:52:23 (Potts)). "[O]ur case law does not require that a particular combination must be the preferred, or the most desirable, combination described in the prior art in order to provide motivation for the current invention." *In re Fulton*, 391 F.3d 1195, 1200 (Fed. Cir. 2004). To the contrary, the Federal Circuit has held that:

> [T]he question is whether there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination, not whether there is something in the prior art as a whole to suggest that the combination is the most desirable combination available.

Id. (internal quotations omitted). As such, the Court concludes that the Gauthier Reference does not teach away from the use of CPE-215 in a testosterone gel, particularly when considered in the context of the Bentley Disclosures, which disclosed that a testosterone gel with CPE-215 had advanced to Phase III clinical trials.

b. CPE-215 Patent Protection

The Court rejects Dr. Lane's testimony that failure by any commercial product to use CPE-215 during the relevant time period indicates that people were not "look[ing]" at CPE-215 and thus that a POSA would not have been motivated to use CPE-215 in a testosterone gel, particularly given the success of AndroGel® (and the Dudley enhancers). (Trial Tr. 6.124:2-4 (Lane)). The '252 and '303 patents protected the use of CPE-215 and other Hsieh enhancers as permeation enhancers through at least 2008. (Trial Tr. 4.48:25-4.49:13 (Potts)). By contrast, the

'894 (Dudley) patent did not specifically claim the use of a class of permeation enhancers, but rather reported a list of permeation enhancers that were known in the prior art. (Trial Tr. 3.113:19-3.114:2 (Potts); DTX-029 at claims 1-42). As such, the fact that "everybody else" had "taken the fatty acid ester or the fatty acid derivative pathway" does not, without more, suggest that a POSA would not have been motivated to use CPE-215 in a testosterone gel.

5. Reasonable Expectation of Success

By April 2001, it was known that testosterone could be used in a transdermal gel. (Trial Tr. 6.87:24-6.89:14 (Lane)). This was an "important discovery" because very few active ingredients were known to be suitable for a transdermal delivery. (*Id*.).

Although a POSA cannot predict whether a given formulation will necessarily be stable without testing it, because the '303 patent teaches that CPE-215 can be combined with steroidal hormones, the Court finds that a POSA would have a reasonable expectation of success in substituting testosterone for clotrimazole in the gel disclosed in Example 25. *See* Trial Tr. 3.130:16-3.132:1, 3.132:18-25 (Potts).

As discussed above, with the exception of polyethylene glycol (PEG), the remaining claimed ingredients—testosterone, a thickening agent, ethanol, glycerin and propylene glycol—and their claimed concentration ranges overlapped with the prior art teaching CPE-215 (the Hsieh Patents and Bentley Disclosures) and testosterone gels (AndroGel®, the '894 (Dudley) patent, and the '919 (Samour) patent). Because the claimed ingredients in the claimed concentrations were known in the art to work with both testosterone gels and CPE-215, this Court concludes that the POSA would have had a reasonable expectation of success in developing the claimed invention. (Trial Tr. 3.131:8-3.132:1; 3.158:19-3.160:13 (Potts)).

In addition, the POSA would have had a reasonable expectation of success in combining

the key ingredients with the finite list of FDA-approved excipients like ethanol, glycerin, propylene glycol, and polyethylene glycol (PEG), that have been known "forever" and had been used "over and over" in compositions in very "similar ways." (Trial Tr. 2.122:8-2.123:11, 2.169:13-20 (Gyurik); Trial Tr. 3.157:7-3.158:6, 3.158:18-3.159:3 (Potts)).

Although the Court agrees with Dr. Lane that formulation science, as a general matter, carries some degree of unpredictability, the Federal Circuit has made clear that "obviousness cannot be avoided simply by a showing of some degree of unpredictability in the art so long as there was a reasonable probability of success." *Allergan, Inc. v. Sandoz Inc.*, 726 F.3d 1286, 1292 (Fed. Cir. 2013) (quoting *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1364 (Fed. Cir. 2007)). Dr. Lane's position that "any change to any component and any change to any amount of a component will have an unpredictable effect on the performance of the gel" lacks support—in the prior art, in data, in evidence introduced at trial or in legal authority—and thus does not convince the Court that any modifications over the prior art were such that a POSA would not have had a reasonable probability of success in formulating the claimed invention. (Trial Tr. 6.83:12-20, 6.84:6-23, 6.85:5-6.86:10 (Lane)). *See, e.g., id.; In re Geisler*, 116 F.3d 1465, 1470 (Fed. Cir. 1997) ("[I]t is not inventive to discover the optimum or workable ranges by routine experimentation."); (Trial Tr. 3.97:19-3.98:8, 3.107:17- 3.108:11, 3.182:4-10 (Potts)) ("[Tweaking the formulation with [] known excipients to achieve optimization is really what a formulator does."); (Trial Tr. 2.155:6-11 (Gyurik)) ("Once again, it wasn't the changes. It was the change. It was from a high PG, high glycerol formula to a very high alcohol, low glycerol, low PG formula")).

To the contrary, based on the evidence in the record, the Court concludes that Watson has met its burden of demonstrating, by clear and convincing evidence, that a POSA had a

reasonable probability of success in developing the patented pharmaceutical formulation based on the prior art teaching CPE-215 (the Hsieh Patents and Bentley Disclosures) and testosterone gels (AndroGel®, the '894 (Dudley) patent, and the '919 (Samour) patent). (Trial Tr. 3.131:8-3.132:1; 3.158:19-3.160:13 (Potts)).

For the reasons set forth above, the Court finds that Watson has made a *prima facie* showing of obviousness.

6. Objective Indicia of Nonobviousness

A prima facie showing of obviousness may be rebutted by objective indicia of nonobviousness, such as copying, long-felt need, failure of others and unexpected results. *See generally KSR*, 550 U.S. at 406. "[O]bjective evidence of nonobviousness must be considered if present." *In re GPAC Inc*., 57 F.3d 1573, 1580 (Fed. Cir. 1995). Moreover, "for objective evidence to be accorded substantial weight, its proponent must establish a nexus between the evidence and the merits of the claimed invention." *Id.*

a. Unexpected Results

As evidence of unexpected results, Auxilium points to a bioequivalence study of AndroGel® and Testim® conducted by Auxilium which unexpectedly found that Testim® had a statistically significant higher absorption rate than AndroGel®.

By way of background, Auxilium sponsored a Phase I clinical trial of Testim®, designated Clinical Study No. AUX-TG-201, that was published as Marbury T. et al., Evaluation of the pharmacokinetic profiles of the new testosterone topical gel formulation, TestimTM, compared to AndroGel®, Biopharmaceutics & Drug Disposition 24:115-120 (2003) (the "Marbury study"). The objective of the Marbury study was "to evaluate the pharmacokinetic profiles after a single dose of a new testosterone topical gel formulation [Testim®] compared to

a commercial testosterone topical gel preparation [AndroGel®]." (DTX-300 at 6). The study was a two-drug, two-period crossover study, meaning that "all subjects got both drugs, one drug on one occasion and one drug on the other occasion." (DTX-300 at 6-7). Blood samples were collected and analyzed to determine various pharmacokinetic measurements, including the maximum observed concentration (Cmax) and the area under the concentration-time curve (AUC0-24). (DTX-300 at 6-8).

There is no dispute that the Marbury study was designed to test the hypothesis of bioequivalence. (DTX-300 at 8-9; 5.61:11-13 (Hamer)). As Dr. Hamer, Watson's expert in biostatistics and clinical trials, explained, "bioequivalence is a kind of a statistical study design[] and associated statistical analysis intended to demonstrate the two formulations behave similarly within the human body." (Trial Tr. 5.55:14-18 (Hamer)). To that end, the study pre-specified that "[i]f the 90% confidence intervals for the measure of relative bioavailability were within the acceptance range of 0.80 to 1.25, then the 2 formulations were judged to be bioequivalent." (DTX-300 at 8).

The Marbury study administered only a single dose of Testim® and AndroGel®, and measured blood concentrations over the next 24 hours. (DTX-300 at 6; Trial Tr. 4.119:23-4.120:14 (Morgentaler)). In the real world, topical testosterone gels "are never prescribed as single doses," rather "they are prescribed as numerous doses over a period of time to achieve steady state." (Trial Tr. 4.153:10-15 (Morgentaler)).

Although the Marbury study was not designed to determine whether Testim® was superior to AndroGel®, its results showed that Testim had a 30% higher absorption rate in both Cmax and AUC0-24 than AndroGel®. The study concluded that the statistical analysis for Cmax and AUC0-24 demonstrated that "the 2 formulations could not be considered

bioequivalent." (DTX-300 at 9). Auxilium had an incentive to find Testim® and AndroGel® were bioequivalent because "if Testim® could be shown to be bioequivalent to AndroGel®, then this could expedite the FDA approval of Testim®" and "[w]ith FDA approval, Testim® could enter the marketplace." (Trial Tr. 5.101:8-13 (Hamer)). Because the investigators of the Marbury Study found that Testim® delivered 30% more testosterone than AndroGel®, the investigators could not declare bioequivalence, which required Auxilium to conduct further clinical studies in order to obtain FDA approval. (Trial Tr. 5.101:8-5.102:11 (Hamer)).

Dr. Morgentaler, Plaintiffs' expert in the field of clinical research and treatment of testosterone deficiency, explained that a substantial number of his patients did not absorb AndroGel® well enough for it to be effective. (Trial Tr. 4.115:21-4.116:10, 4.116:24-4.118:8, 4.119:15-17 (Morgentaler)). Nevertheless, Dr. Morgentaler testified that in his clinical practice he prescribes more AndroGel® to his patients than Testim®. (Trial Tr. 4.164:8-11, 4.165:22-24 (Morgentaler)).

Given: (1) that none of Plaintiffs' experts testified that Testim® exhibited unexpected results;[14] (2) that the Marbury Study was admittedly designed to test bioequivalence and not superiority, (3) that the FDA has concluded that AndroGel® and Testim® are "generally comparable" in their ability to replace testosterone,[15] and (4) Dr. Morgentaler's concession that he continues to prescribe more AndroGel® to his patients than Testim® (notwithstanding Testim's alleged superiority), the Court concludes that Testim® exhibits no unexpected results.

[14] (Trial Tr. 5.152:19-21 (Levin); Trial Tr. 4.139:7-9 (Morgentaler)).

[15] (DTX-289 at 6; Trial Tr. 4.159:7-4.160:19 (Morgentaler)).

b. Long-Felt but Unmet Need and Failure of Others

"Long-felt need is closely related to the failure of others. Evidence is particularly probative of obviousness when it demonstrates both that a demand existed for the patented invention, and that others tried but failed to satisfy that demand." *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.*, 676 F.3d 1063, 1082 -1083 (Fed. Cir. 2012).

By April 2001, AndroGel® "was the most common form of treatment" for testosterone deficiency. (Trial Tr. 4.116:15-18 (Morgentaler)). AndroGel® was "effective for many men." (Trial Tr. 4.166:21-23 (Morgentaler)). Indeed, "AndroGel has helped many patients achieve the desired serum testosterone levels." (Trial Tr. 4.140:24-4.141:1 (Morgentaler)).

It is undisputed that two years passed between the approval of AndroGel® in February 2000 and the priority date of the claimed invention of April 2002. (DTX-074 at 1 (AndroGel® was approved by the FDA on February 28, 2000.); DTX-004 at 2 (The '607 patent claims priority to the '103 provisional application filed on April 19, 2002); Trial Tr. 4.144:2-5 (Morgentaler)). Morgentaler conceded that "the two years between the launch of AndroGel to the date of the invention is not a long time to have an unmet need." (Trial Tr. 4.144:6-9 (Morgentaler)). As such, the Court concludes that any need that AndroGel® allegedly failed to fill was not "long-felt."

The Court also finds no evidence of failure of others. In particular, the Court finds that Dr. Hsieh's testosterone gels were not failures. (Trial Tr. 3.172:20-3.173:7 (Potts)). To the contrary, testimony at trial indicated that Dr. Hsieh died unexpectedly in an automobile accident in 1995, while he was still in the process of commercializing a testosterone gel. (Trial Tr. 1.142:13-17 (Hsieh); 4.176:5-10 (Murphy); Trial Tr. 3.57:13-16 (Gyurik); Trial Tr. 3.172:20-

3.173:7 (Potts)). In particular, as stated above, as of January 25, 1995, Dr. Hsieh was still working with ALZA on a joint venture to develop a permeation enhanced testosterone gel. In August 1994, Conrex and ALZA executed a Material Evaluation Agreement to test Conrex's CPE-215 (the "Material") with, *inter alia*, testosterone. On January 25, 1995, ALZA sent Conrex, as well as "several key individuals at ALZA," the results of its skin flux studies of Conrex's testosterone formulations, which revealed that the two testosterone gels with CPE-215 (T-2 J2574 and T-4 J2574) exhibited greater flux (rate of speed of drug delivery) across the skin than the gel formulation without CPE-215 (T-0 J2574) at each of the time points measured over the course of 64 hours. As discussed above, no instability was reported in ALZA's January 1995 results of its permeation studies of Dr. Hsieh's testosterone gels. (DTX-211 at 64-66). No evidence was introduced at trial suggesting that Dr. Hsieh had abandoned his work on his testosterone formulations between January 25, 1995 and the time of his death (at some unspecified point later that year).

Dr. Gauthier did not fail in preparing a testosterone gel using CPE-215 as a permeation enhancer. Indeed, Dr. Gauthier did not even prepare a testosterone gel with CPE-215; instead, he prepared a testosterone solution with CPE-215. Moreover, the evidence introduced at trial did not establish that Dr. Gauthier's research was even *aimed* at developing a transdermal testosterone gel product using CPE-215 as the permeation enhancer. (Trial Tr. 6.189:24-6.190:4 (Gauthier) ("Q. Was the research at page 97 of your thesis aimed at potential commercial drug formulations? A. For SEPA [MachroChem's permeation enhancer]. For other enhancers [i.e., CPE-215], it is possible, but I do not recall . . . .")).

As such, the Court concludes that there is no evidence of failure of others. *See, e.g.*, *Ormco Corp. v. Align Tech., Inc*., 463 F.3d 1299, 1313 (Fed. Cir. 2006) (finding no evidence of

failure of others where "the evidence does not suggest that these prior attempts failed because the devices lacked the claimed features.").

d. Copying

Plaintiffs maintain that Watson's act of copying the formulation of claim 3 of the '607 patent serves as evidence of non-obviousness.

By way of background, when Watson began its development of a generic Testim® formulation, it initially built on its own generic AndroGel® formulation. (Trial Tr. 3.204:12-16, 4.44:25-4.45:5, 4.45:9-13 (Potts)). Eventually, however, Watson chose to reformulate its testosterone gel product with the goal of achieving a Q1/Q2 generic formulation so that Watson's generic product would be AB rated by the FDA and would thus be recognized as a generic equivalent to Testim® on the market. (Trial Tr. 6.13:23-6.14:11 (Gwinn)); Trial Tr. 5.188:18-5.193:16 (Rifaat)).

Having carefully considered Plaintiffs' copying-related arguments and the evidence introduced at trial, the Court does not find compelling Plaintiffs' evidence of copying in the context of this ANDA case where "a showing of bioequivalency is required for FDA approval." *Purdue Pharma Prods. L.P. v. Par Pharm., Inc.*, 377 Fed. Appx. 978, 983 (Fed. Cir. 2010).

7. Conclusion

For the reasons set forth above, the Court concludes that Watson has made a prima facie showing that claim 3 of the '607 patent would have been obvious in view of the '252 and '303 (Hsieh) patents, the Bentley Disclosures, the '894 (Dudley) patent, and the '919 (Samour) patent. The Court also finds that the Plaintiffs' evidence of secondary considerations is inadequate to raise any doubt as to the obviousness of claim 3 of the '607 patent.

Based on the aforesaid findings by this Court, the Court need not determine whether claim 3 of the '607 patent is also invalid for derivation and/or improper inventorship, or otherwise unenforceable due to inequitable conduct. Nevertheless, the Court will proceed in its analysis for purposes of completeness.

B. Derivation and Improper Inventorship

Pursuant to § 102(f), a patent is invalid if the inventors named in the patent did not actually invent the claimed invention. 35 U.S.C. § 102(f). One cannot claim or reproduce the invention of another and obtain a patent on that "invention." *OddzOn Prods., Inc. v. Just Toys, Inc.*, 122 F.3d 1396, 1401–02 (Fed. Cir. 1997).

1. Derivation: Conception and Communication

"To show derivation, the party asserting invalidity must prove both prior conception of the invention by another and communication of that conception to the patentee." *Gambro Lundia AB v. Baxter Healthcare Corp.*, 110 F.3d 1573, 1576 (Fed. Cir. 1997). In light of this standard, this Court has previously held that the question here is whether the formulation in the Permeation Studies enabled one of ordinary skill in the art to formulate the patented invention.

"Conception is 'the formation in the mind of the inventor, of a definite and permanent idea of the complete and operative invention, as it is hereafter to be applied in practice.' " *Solvay S.A. v. Honeywell Int'l, Inc.*, 622 F.3d 1367, 1377 (Fed. Cir. 2010). "An idea is sufficiently definite and permanent for conception if it provides one skilled in the art with enough guidance to 'understand the invention,' that is, 'when the inventor has a specific, settled idea, a particular solution to the problem at hand, not just a general goal or research plan he hopes to pursue.' . . . Thus, with regard to a claimed chemical compound, conception requires that the inventor 'be

able to define' the compound 'so as to distinguish it from other materials, and to describe how to obtain it.' " *Invitrogen Corp. v. Clontech Labs., Inc.*, 429 F.3d 1052, 1063 (Fed. Cir. 2005). "[A] finding of conception does not require perfection: conception is complete when 'the idea is so clearly defined in the inventor's mind that only ordinary skill would be necessary to reduce the invention to practice, without extensive research or experimentation.' " *Spansion, Inc. v. Int'l Trade Com'n*, 629 F.3d 1331, 1356 (Fed. Cir. 2010) (citing *Burroughs Wellcome Co. v. Barr Labs., Inc*., 40 F.3d 1223, 1228 (Fed. Cir. 1994)). In other words, "an inventor need not know that his invention will work for conception to be complete. He need only show that he had the idea." *Burroughs Wellcome Co. v. Barr Labs., Inc.*, 40 F.3d 1223, 1228 (Fed. Cir. 1994); *see also Apotex Inc. v. Cephalon, Inc*., 2011 WL 6090696, at *18 (E.D. Pa. 2011) ("[T]he original inventor must have understood the features of his invention, however, the original inventor need not recognize his 'invention in the same terms as those recited in the [claims]' as the invention is not the claim language, but, rather, the subject matter of those claims.") (citations omitted), *aff'd*, 500 Fed. Appx. 959 (Fed. Cir. 2013), *cert. denied*, —— U.S. ——, 134 S.Ct. 825, 187 L.Ed.2d 686 (2013). Finally, it should be noted that "an inventor's testimony, standing alone, is insufficient to prove conception. Conception requires corroboration of the inventor's testimony." *Gambro*, 110 F.3d at 1576.

As to the second prong, the Court must assess "whether the communication enabled one of ordinary skill in the art to make the patented invention." *Gambro*, 110 F.3d at 1578 ("If the proposal does not disclose recalibration during dialysis, it cannot serve as the basis for a communication of that idea.").

2. Improper Inventorship

As stated above, pursuant to § 102(f), a patent is invalid if the inventors named in the patent did not actually invent the claimed invention. 35 U.S.C. § 102(f). "When a party asserts invalidity under § 102(f) due to nonjoinder, a district court should first determine whether there exists clear and convincing proof that the alleged unnamed inventor was in fact a co-inventor. Any testimony from a person claiming inventorship status "must be corroborated by independent evidence." *Cooper v. Goldfarb*, 154 F.3d 1321, 1330 (Fed. Cir. 1998). Independent, corroborating evidence is required "to prevent fraud, by providing independent confirmation" of the alleged "inventor's testimony." *Kridl v. McCormick*, 105 F.3d 1446, 1450 (Fed. Cir. 1997). Further, the corroboration requirement is necessary because years after the issuance of a patent, even "honest witnesses can convince themselves that they conceived the invention of a valuable patent." *Price v. Symsek*, 988 F.2d 1187, 1195 (Fed. Cir. 1993).

Upon such a finding of incorrect inventorship, a patentee may invoke section 256 to save the patent from invalidity. *See* 35 U.S.C. § 256 ("Whenever through error a person is . . . not named in an issued patent and such error arose without any deceptive intention on his part, the Director may . . . issue a certificate correcting such error."). "Nonjoinder may be corrected 'on notice and hearing of all parties concerned' and upon a showing that the error occurred without any deceptive intent on the part of the unnamed inventor." *Pannu v. Iolab Corp*., 155 F.3d 1344, 1350 (Fed. Cir. 1998). "If a patentee demonstrates that inventorship can be corrected as provided for in section 256, a district court ***must*** order correction of the patent, thus saving it from being rendered invalid." *Pannu*, 155 F.3d at 1350 (emphasis added). "While lack of deceptive intent, as a negative, may be hard for a patentee to prove when it claims relief under

the statute, good faith is presumed in the absence of a persuasive showing of deceptive intent." *Pannu*, 155 F.3d at 1351 n. 4.

3. Analysis

Having carefully considered the testimony of the witnesses at trial and the evidence introduced at trial, the Court concludes that the formulation(s) contained in the Permeation Studies enabled one of ordinary skill in the art to formulate the patented invention. In particular, the Court finds that conception of the invention in this case occurred, at the latest, in July 1994, when Dr. Hsieh created a formulation for a testosterone gel comprised of the following key ingredients: an androgen, a Hsieh enhancer, and a thickening agent. *Compare* Abstract of '607 patent (reciting a "pharmaceutical composition comprising: (A) an androgen, (B) a cyclic enhancer of the type used in the compositions and methods claimed by U.S. Pat. No. 5,023,252 to Hsieh, and and (C) a thickening agent.") (DTX-4 at 2) *with* DTX 147. Although Dr. Hsieh is deceased and thus could not testify at trial, his Permeation Studies—and, in particular, the data from his July 20, 1994 permeation study—showed that over the course of 24 hours "all three compositions containing the [CPE-215] permeation enhancer, the 2, 4, and 8 percent, show substantially greater transport of testosterone through hairless mouse skin, and in particular, the composition containing 8 percent, the TC8, shows the highest transport of all three." (DTX-147 at 6; Trial Tr. 3.136:1-19 (Potts)). These promising results were confirmed by the ALZA study and later by Mr. Murphy's own interpretation of the results of the ALZA study. *See* DTX-211 at 66 (containing correspondence from ALZA to Conrex recognizing that the two testosterone gels with CPE-215 exhibited greater rate of speed of drug delivery across the skin than the gel formulation without CPE-215); Trial Tr. 3.138:19-3.141:5 (Potts); DTX-211 at 63 (containing correspondence from Mr. Murphy to ALZA seeking to restart the collaborative venture it

previously had with Conrex in developing Dr. Hsieh's testosterone gels and recognizing that the studies conducted by ALZA had indicated "significant activity" in enhancing the delivery of testosterone).

Although Dr. Hsieh died before his formulations became pharmaceutical compositions, as stated above, a finding of conception does not require perfection. "[C]onception is complete when 'the idea is so clearly defined in the inventor's mind that only ordinary skill would be necessary to reduce the invention to practice, without extensive research or experimentation.' " *Spansion,* 629 F.3d at 1356; *see also Burroughs,* 40 F.3d at 1228 ("[A]n inventor need not know that his invention will work for conception to be complete. He need only show that he had the idea."). The Court finds that Dr. Hsieh's idea—of creating a testosterone gel formulation combining an androgen, a Hsieh enhancer and thickening agent—was so clearly defined in Dr. Hsieh's mind, as evidenced in his July 1994 Permeation Studies and in his correspondence with ALZA, that only ordinary skill would have been necessary to reduce the invention to practice, without extensive research or experimentation. *See Spansion,* 629 F.3d at 1356. In particular, the Court is persuaded by testimony by Dr. Potts, wherein he opined that Dr. Hsieh's Permeation Studies, with "minor tweaks known to persons of skill in the art," would have "absolutely enabled" the POSA to formulate the claimed invention. (Trial Tr. 3.186:25-187:15, 3.189:6-9 (Potts)). In support of his opinion, Dr. Potts explained that the only explicit difference between the claimed gels and Dr. Hsieh's testosterone gels are a higher amount of ethanol, and in some claims, the addition of polyethylene glycol (PEG). (DTX-004 at claim 3; DTX-147 at 3-4; see Trial Tr. 3.153:8-3.154:11, 3.157:6-20 (Potts)). Dr. Potts explained that adjusting the amount of ethanol is "the kind of tweaking that a formulator would do routinely day in and day out in their efforts to optimize [a] formulation." (Trial Tr. 3.188:7-21 (Potts); *see* DTX-008 at claim 1

(Claim 1 recites that the amount of ethanol in the claimed composition may range from about 40%-80%.)). As the POSA "increase[s] one solvent," such as ethanol, she would make a "concomitant decrease in glycerin and propylene glycol [the other solvents], so it still gives you 100 percent composition." (Trial Tr. 3.154:3-11 (Potts)). Dr. Potts further explained that "it was well-known that polyethylene glycol had desired properties in the formulation of these transdermal gels and products." (Trial. Tr. 3.158:3-14 (Potts)). As such, Dr. Potts opined—and this Court agrees—that "Dr. Hsieh's contributions were the vast majority of the contribution," and that Mr. Gyurik's seventeen days-worth of work "was a simple tweaking of an already existing formulation." (Trial Tr. 3.191:11-18 (Potts)).

The Court also finds that Dr. Hsieh's idea—of creating a formulation for a testosterone gel comprised of the following key ingredients: an androgen, a Hsieh enhancer, and a thickening agent—was communicated to the patentee, Bentley, when it acquired the Conrex materials—i.e., the two to five boxes, which contained, among other things, Dr. Hsieh's laboratory notebook. In fact, Mr. Gyurik's own testimony and contemporaneous notes (dated April 18, 2000) confirm that he started his "first experiment with a testosterone gel at Bentley" by following the directions Dr. Hsieh recorded in his laboratory notebook. (Trial Tr. 2.40:7-22 (Gyurik)); 6.160:24-6.161:4 (Lane)); (DTX-146 at 20).

Accordingly, the conception of a formulation for a testosterone gel comprised of the following key ingredients: an androgen, a Hsieh enhancer, and a thickening agent, by Dr. Hsieh, *and* communication of that invention to Bentley (on or before April 2000), renders claim 3 of the '607 patent (filed in April 2002)[16] invalid for derivation under § 102(f). *See, e.g., Apotex Inc. v.*

[16] The earliest patent application to which the '607 patent claims priority is U.S. Provisional Patent Application No. 60/374,103 ("the '103 provisional application") filed on April 19, 2002.

Cephalon, Inc., 2011 WL 6090696, at *21 (E.D. Pa. 2011) (finding patent-in-suit invalid for derivation by virtue of "the conception of the chemical compound possessing the properties claimed in the patent by Lafon, and Lafon's communication of that chemical compound and its specific properties to Cephalon no later than July 1993"), *aff'd*, 500 Fed. Appx. 959 (Fed. Cir. 2013), *cert. denied*, —— U.S. ——, 134 S.Ct. 825, 187 L.Ed.2d 686 (2013); *see generally Pannu*, 155 F.3d at 1349-50 ("Thus, section 102(f) still makes the naming of the correct inventor or inventors a condition of patentability; failure to name them renders a patent invalid.").

The Court is not persuaded by Plaintiffs argument that there can be no derivation where there is common ownership of the patent and the technology from which the patent was allegedly derived at the time of the "invention of the patent." (Pl.'s Post Tr. Br. at 40). In other words, Plaintiffs argue that Watson has failed to demonstrate conception of the invention "by another," inasmuch as Bentley allegedly owned the data from which claim 3 of the '607 was allegedly derived at the time the '607 patent was issued. As discussed above, however, the Court finds that the conception of the invention in this case—Dr. Hsieh's creation of a formulation for a testosterone gel comprised of the following key ingredients: an androgen, a Hsieh enhancer, and a thickening agent—occurred in 1994, well before Bentley acquired Conrex (in December 1998). Although Plaintiffs are correct in noting the absence of legal authority addressing this discrete issue, the Court finds instructive the Federal Circuit's decision in *Gambro*, 110 F.3d 1573.

In *Gambro*, the patentee alleged infringement by a competitor, Baxter Healthcare, of its patent for recalibrating sensors during kidney dialysis to accurately measure impurities removed a patient's blood. In defense, Baxter asserted, among other things, the invalidity of the patent-in-suit for derivation. In particular, Baxter argued that the patent-in-suit had been derived from technology that Gambro had purchased from Repgreen, a British bioengineering company. In

reversing the district court's finding of derivation, the Federal Circuit never held that derivation did not apply in that context because there was common ownership of the patent and the technology from which the patent was allegedly derived at the time the patent-in-suit was issued. Stated differently, the Federal Circuit did not conclude that Baxter had failed to meet its burden of demonstrating conception of the invention by "another" based on common ownership at the time of patenting, despite the existence of same. To the contrary, the Federal Circuit held that Baxter's interpretation of a single "ambiguous" passage of a document left in the Repgreen file when it was acquired by Gamrbo lacked sufficient support to corroborate testimony regarding conception of the invention by the author of the document (i.e., the allegedly "unnamed" inventor).

Thus, absent any legal authority to the contrary, this Court concludes that common ownership of the patent and the technology from which the patent was allegedly derived at the time of patenting does not preclude a finding of derivation where conception of the invention occurred prior to the common ownership.

Even assuming, *arguendo*, that the patent-in-suit were not invalid under the doctrine of derivation, the Court finds that Watson has proven, by clear and convincing evidence that Dr. Hsieh was, *at a minimum*, a co-inventor of the '607 patent. "Inventors may apply for a patent jointly even though (1) they did not physically work together or at the same time, (2) each did not make the same type or amount of contribution, or (3) each did not make a contribution to the subject matter of every claim of the patent." *Pannu*, 155 F.3d at 1351. Rather, "all that is required of a joint inventor is that he or she (1) contribute in some significant manner to the conception or reduction to practice of the invention, (2) make a contribution to the claimed invention that is not insignificant in quality, when that contribution is measured against the

dimension of the full invention, and (3) do more than merely explain to the real inventors well-known concepts and/or the current state of the art." *Id.* Again, even assuming that the patent-in-suit were not invalid for derivation, the Court concludes that, at a minimum, Dr. Hsieh—by virtue of his Permeation Studies and the data underlying same—contributed in a significant manner to the conception of the invention and thus was a co-inventor of the '607 patent.

Because there has been no showing of any deceptive intent on behalf of Dr. Hsieh, the "unnamed" inventor, § 256 would generally afford Plaintiffs the opportunity to save the '607 patent from invalidity due to improper inventorship. *See Pannu*, 155 F.3d at 1350 ("Nonjoinder may be corrected 'on notice and hearing of all parties concerned' and upon a showing that the error occurred without any deceptive intent on the part of the unnamed inventor."). Having already determined, however, that claim 3 of the '607 patent is invalid as obvious, Plaintiffs' attempt to save the '607 patent by correcting its inventorship pursuant to § 256 would be futile. For the same reason, the Court also declines to weigh in on the related question of whether invalidity due to derivation can be corrected pursuant to § 256. *Cf. Gambro*, 110 F.3d at 1578 ("Because this court reverses the district court's ruling of invalidity based on derivation, it need not reach the issue of correction of inventorship under 35 U.S.C. § 256 (1994).").

II. Patent Unenforceability

Watson also claims that the '607 patent is unenforceable due to inequitable conduct. In particular, Watson claims that Mr. Gyurik committed inequitable conduct by: (1) failing to disclose to the PTO the existence of the "Permeation Studies," and (2) by submitting a false declaration to the PTO indicating that he was the sole inventor of the '607 patent.

A. Inequitable Conduct

"To prevail on a claim of inequitable conduct, the accused infringer must prove that the patentee acted with the specific intent to deceive the PTO. . . In other words, the accused infringer must prove by clear and convincing evidence that the applicant knew of the reference, knew that it was material, and made a deliberate decision to withhold it." *Therasense, Inc. v. Becton, Dickinson and Co.*, 649 F.3d 1276, 1290 (Fed. Cir. 2011). The Federal Circuit also recognized an exception to the "but for" standard in cases of "affirmative acts of egregious misconduct, such as the filing of an unmistakably false affidavit." *Id.* at 1292.

"Because direct evidence of deceptive intent is rare, a district court may infer intent from indirect and circumstantial evidence. However, to meet the clear and convincing evidence standard, the specific intent to deceive must be 'the single most reasonable inference able to be drawn from the evidence.' " *Id.* at 1290. "Because the party alleging inequitable conduct bears the burden of proof, the "patentee need not offer any good faith explanation unless the accused infringer first ... prove[s] a threshold level of intent to deceive by clear and convincing evidence." The absence of a good faith explanation for withholding a material reference does not, by itself, prove intent to deceive." *Id.* at 1291. Finally, if the accused infringer "prove[s] both elements—intent and materiality—by clear and convincing evidence," the court must still "weigh the equities to determine whether the applicant's conduct before the PTO warrants rendering the entire patent unenforceable." *Id.* at 1287.

1. Materiality

Watson claims that the Permeation Studies are "but for" material to patentability because they render the asserted claim invalid as obvious (as § 102(b) prior art) and as evidence of derivation and incorrect inventorship under § 102(f)). This Court has now held, however, that

the Permeation Studies do not qualify as § 102(b) prior art for purposes of obviousness. This Court also held, in its July 8, 2014 summary judgment Opinion, that "incorrect inventorship evidence is not but-for material under *Therasense* because, according to the patent statute, inventorship can be corrected as long as there was no deceptive intent on the part of the unnamed inventor." July 8, 2014 Opinion at 13-14. Watson cites to no binding legal authority for the proposition that evidence of derivation, which is not found to be § 102(b) prior art, can nevertheless be considered "but for" material to patentability, particularly in light of § 256. *See generally Chou v. Univ. of Chicago*, 254 F.3d 1347, 1358 (Fed. Cir. 2001) ("We have previously interpreted § 256 broadly as a 'savings provision' to prevent patent rights from being extinguished simply because the inventors are not correctly listed."). As such, the Court finds that the Permeation Studies do not satisfy the "but for" materiality standard.

Watson also maintains that the allegedly false declarations submitted to the PTO by Mr. Gyurik constitute affirmative acts of egregious misconduct that were *per se* material to patentability under *Therasense*, 649 F.3d at 1292 (recognizing an exception to the "but for" standard in cases of "affirmative acts of egregious misconduct, such as the filing of an unmistakably false affidavit."). Having now determined that the '607 patent was, in fact, derived from Dr. Hsieh's Permeation Studies (and their corresponding data), and thus that Dr. Hsieh was—*at a minimum*—a co-inventor of the '607 patent, the Court finds that the declarations submitted by Mr. Gyurik to the PTO indicating that he was the "original, first and sole inventor . . . of the subject matter which is claimed" in the '607 patent were false. *See, e.g.*, DTX-011 at 157. It follows that Mr. Gyurik's filing of the false affidavits constitutes affirmative acts of egregious misconduct, which are *per se* material to patentability under *Therasense*, 649 F.3d at 1292.

2. Intent to Deceive

In addition to the materiality prong, Watson must also prove by clear and convincing evidence that the actors in question acted with the specific intent to deceive the PTO. *Id.* at 1290. It is not enough to establish that the patent applicant had a generalized intent to deceive or withhold. Rather, under *Therasense*, a "specific intent" to deceive must be proven by demonstrating by clear and convincing evidence "that the applicant knew of the reference, knew that it was material, and made a deliberate decision to withhold it." *Id.* at 1290. To meet the clear and convincing evidence standard, the specific intent to deceive must be the single most reasonable inference able to be drawn from the evidence." *Id.* Under *Therasense*, where "there are multiple reasonable inferences that may be drawn, intent to deceive cannot be found." *Id.* at 1290-91.

The Court begins by noting that Watson has not shown any direct evidence of deceptive intent by Mr. Gyurik. Having carefully considered the circumstantial evidence adduced at trial, the Court finds that although it could be reasonable to infer that Mr. Gyurik's failure to disclose proper inventorship of the patent-in-suit was due to financial motive (i.e., his membership on Bentley's Board of Directors and the royalty provision originally contained in the Asset Purchase Agreement requiring Bentley to pay out 5% in royalties if a product was actually developed from Dr. Hsieh's work), or personal pride,[17] the Court is not convinced that this is the single *most reasonable* inference to be drawn from the evidence. To the contrary, the Court finds that it is equally reasonable to infer, based on Mr. Gyurik's testimony at trial and his contemporaneous

[17] *See, e.g.*, DTX-143 at 1 (containing e-mail written by Mr. Gyurik in July 2008, wherein he describes himself as "the only one in the world who has a patented and commercialized true permeation enhancing formulation (Testim, and soon Nasulin) as well as a worldwide patented and marketed antiparasitic drug (Albenza, GSK).").

laboratory notebook, that it was, in fact, his subjective belief that Dr. Hsieh's testosterone gel formulations were failures given the physical instability (i.e., "big glob") he detected in his reproduction of Dr. Hsieh's TC-4 formulation.[18] (Trial Tr. 2.46:12-17, 2.47:24-2.49:11, 2.81:6-19 (Gyurik)); (DTX-146 at 20). Because there are, at a minimum, *multiple* reasonable inferences that may be drawn from the evidence, the Court finds that Watson has failed to meet its burden of demonstrating, by clear and convincing evidence, that Mr. Gyurik acted with the specific intent to deceive the PTO when he represented that he was the "original, first and sole inventor . . . of the subject matter which is claimed" in the '607 patent. *See Therasense*, 649 F.3d at 1290-91. As such, the Court finds no inequitable conduct.

CONCLUSION

For the reasons stated above, the Court concludes that claim 3 of the '607 patent is invalid for obviousness, derivation and/or improper inventorship. No finding of inequitable conduct shall issue.

This Court's Opinion will be filed under temporary seal. The Opinion will be unsealed on Monday, January 5, 2015 unless an appropriate motion to seal same (pursuant to Local Civil Rule 5.3(c)) is filed by either side by January 2, 2015.

An appropriate Order accompanies this Opinion. Counsel are hereby directed to submit a proposed form of judgment consistent with this Opinion.

s/ Jose L. Linares
Jose L. Linares
United States District Judge

Date: December 16, 2014

[18] The Court makes this finding notwithstanding the fact that Mr. Gyurik used data from Dr. Hsieh's Permeation Studies to support regulatory approval of Testim® by the UK health authorities, as discussed in greater detail above. (DTX-153 at 2).